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Section of Dermatology.

[*November* 19, 1931.]

Erythema Perstans.—W. KNOWSLEY SIBLEY, M.D.

Florence H., a domestic servant, single, aged 40.

Present attack began five or six months ago. Since 1921 patient has had several attacks lasting about two months, with intervals of about one year. The lesions were then confined to the upper arms only, and appeared symmetrically. Four years ago a breast was removed on account of adenoma.

Present condition.—The lesion begins as a minute papule and grows rapidly to the size of a half-crown piece in one week. At present there is such a lesion on the upper part of the left thigh which presents an irregular, but roughly circular, erythematous patch about 1 in. in diameter with a paler violaceous ring and a fine, scaly centre. There is then a normal zone of skin about a quarter of an inch wide which in turn is bounded by a slightly raised, non-scaly, pale red-brick coloured irregular ring about one-tenth of an inch wide, appearing as a halo outside the lesion.

On the anterior surface of the right leg there is a large patch which is said to be six months old, forming almost a complete circle, but the rings are incomplete, and the broken ends of the circle curl inwards. The central zone is of normal colour. The wide central erythemato-squamous zone is about one inch in diameter and the outer ring, which is one-tenth of an inch wide, shows no appreciable elevation. On the upper arm, and chiefly on the extensor aspect, there are numerous rings which, coalescing, form serpiginous figures. Since the patient has been under observation the lesions in the arms have faded considerably, while those in the legs have become more marked.

Histological report (Dr. I. K. Muende).—There is very little spongiosis in the epidermis, and in one zone slight parakeratosis. There is some œdema of the pars papillaris, with widening of the papillæ and considerable dilatation of the blood-vessels and lymphatic spaces, around which is found a sparse lymphoid infiltration.

Discussion.—The PRESIDENT said he did not think that he had ever before seen an eruption of that type which had such persistently scaly lesions. The scales were thick and firm round the edge, otherwise there was a resemblance to erythema perstans. In other cases of the condition, however, his experience had been that the scaling was a late feature, relatively slight in amount, and easily removed. He did not know whether Dr. Sibley would class this as Darier's centrifugal erythema, or whether he regarded that as distinct from it.

Dr. KNOWSLEY SIBLEY, in reply, said that this case was probably more or less similar to centrifugal erythema of Darier. He wondered whether it should be described as erythema figuratum perstans. The latter was supposed to occur only on the trunk, whereas this eruption was practically confined to the limbs.

Dr. H. W. BARBER said that he had had under observation some months a case exactly like this, but more extensive. Though the lesions had the configuration and the evolution of erythema perstans, they were not purely erythematous. The edges were almost vesicular, and they dried up with a very definite firm scale. He did not know how to classify his own case, but he was sure it was not a simple erythema.

(1) Lichen Planus, Lichen Spinulosus and Cicatricial Alopecia. (2) Lichen Scrofulosorum. (3) Micro-sporide simulating Lichen Spinulosus.—Sir ERNEST GRAHAM-LITTLE, M.D.

In all these three cases the clinical type which we may call lichen spinulosus exists, but each of the three has a different causation. In the first there was a patch of cicatricial atrophy on the scalp, and a very definite eruption of lichen plano-pilaris on the trunk, and there were some isolated lesions, definitely lichen planus, on the arms and on the upper part of the trunk. There was, at first, no lichen planus of the mouth; that appeared about July, 1931. The lichen plano-pilaris developed first on the scalp, and the hair was denuded on that part. I have seen cases of cicatricial atrophy of the scalp with a history of lichen plano-pilaris more than once, but the plano-pilaris part of it usually disappears more rapidly. I showed another case this afternoon, that of a girl who had extensive cicatricial atrophy of the scalp, but she has no lesions of lichen planus at the present time, though she gives a history of having had an itchy red eruption of the arms and thighs, which disappeared five years ago. The scalp condition has persisted.

In the second case the condition is almost certainly lichen scrofulosorum. There is much less marked spiny eruption, with typical circumscribed patches, and with the histology of lichen scrofulosorum.

In the third case the eruption followed upon microsporon infection of the scalp; there is an extensive follicular spiny eruption on the trunk, which has persisted over two months. It is now fading.

Discussion.—Dr. H. W. BARBER asked whether Sir Ernest agreed with him that most cases of Brocq's pseudo-pelade were really lichen planus of the scalp.

With regard to the case of lichen scrofulosorum, he did not doubt the diagnosis, but Dr. Forman and he had recently had a series of cases which, clinically, he would have diagnosed as lichen scrofulosorum, but which gave a negative intradermal reaction to tuberculin, and very strong intradermal reactions with streptococcal emulsion. Many cases diagnosed as lichen scrofulosorum were lichenoid streptococcides, such as Dr. Whitfield had described in association with impetigo of the scalp. If children with chronic streptococcal lesions—impetigo, fissures, intertrigo—were examined, they were often found to have these lichenoid lesions on the trunk and limbs, and the speaker thought there was a lichenoid streptococcide which must be carefully differentiated from lichen scrofulosorum.

Dr. MACLEOD asked if the ringworm had been under treatment with strong irritants, as his experience had been that microsporidia occurred chiefly in three types of cases: (1) In microsporon kerion; (2) after defluvium by X-rays, especially if the defluvium were imperfect, and (3) when the scalp had been irritated by treatment. He had not so far seen any cases of untreated or slightly treated microsporon ringworm of the scalp of the usual slightly inflammatory type associated with microsporid eruptions.

Sir ERNEST GRAHAM-LITTLE (in reply) said he agreed with Dr. Barber; he regarded Brocq's pseudo-pelade as a terminal phase of, possibly, several kinds of disorder, and lichen planus was becoming more frequently recognized as a cause of that end-product. With regard to the microsporide, he had never seen an eruption of lichen spinulosus in microsporon infection, but the rash was the first thing noted in his case. Therefore probably the child had had no treatment until seen in the department of the hospital, to which she went because of the rash.

Arsenical Pigmentation of Unusual Extent and Severity in a Case of Pruriginous Dermatitis of the Besnier Type.—H. SEMON, M.D.

Miss D., aged 31.

Since 1921 has suffered from almost continual irritation in the bends of the elbows and fronts of the wrists, symmetrically. Gradual spread to arms and face in 1927, and after that date to upper part of chest, and back. Always aggravated by cold winds and heat of the fire, but not by sun, in fact, the seaside seemed to benefit the condition.

No history of eczema or asthma in the family. Patient herself is not asthmatic.

When first seen by exhibitor, January 28, 1930, there was a subacute irritable dermatitis on the face and neck, and in the flexures of the joints. There was *no abnormal pigmentation*, and no weeping. There were no characteristic lesions of any kind, and the picture was that due to violent scratching and rubbing, with a tendency to lichenification.

Previous treatment had included small doses of Fowler's solution (2 minims three times a day), but not for more than about a month, as the drug was not well tolerated, and appeared to increase the irritation. No mention was made of this observation at the time of the first consultation, and a course of sodium cacodylate (Clin.) by hypodermic injection was advised. Only seven injections in all were given. (Total arsenic, $2\frac{5}{8}$ gr.)

When seen a second time in December, i.e., eleven months later, all the pruriginous areas had assumed the dark mottling now apparent, and there was no improvement in the pruritus, which was exceedingly severe. Under a course of whole blood injections this symptom has greatly improved in the current year, but the pigmentation persists.

Histological examination of a section of the skin of the back clearly reveals marked brownish and brownish green pigment lying in the chromatophore cells in the upper-third of the subcutis. The basal cell-layer also contains this, but not to the same degree. There is no free pigment ; it is all intracellular. Chemical tests have proved it to be melanin, and the microscopical evidence thus supports the diagnosis made on the clinical symptoms.

The long period—according to the practitioner, about a year—which intervened between the arsenical injections and the appearance of the pigmentation should be noted, but it is not, I believe, an altogether unknown feature in the sequence.

Discussion.—The PRESIDENT said that Dr. O'Donovan had published the report of a case in which there was intense pigmentation following arsenical dermatitis due to the use of salvarsan. He (the speaker) wondered how far the inflammation of the skin played a part in causing this pigmentation, and whether there had been friction. [Dr. SEMON : "Yes."]

Dr. H. MACCORMAC referred to a case, under his care, of exfoliative dermatitis not following arsenic ; the patient's skin became pigmented as in Dr. O'Donovan's case, and was probably due to melanin ; the pigmentation was thus a sequel of the exfoliative process and unconnected with any drug.

Unilateral Vascular Nævus (Angio-elephantiasis).—A. M. H. GRAY, C.B.E., M.D. (President).

This case is under the care of Mr. Gwynne Williams, by whose kind permission I am showing it.

The patient, a woman, aged 31, has had lumps on the left upper limb, especially on the hand, since the age of 9 years : they came on gradually, sometimes being painful and itchy. The lesions are confined to the left side of the chest and back, and the left upper limb. They consist of swellings, some subcutaneous, and some

involving the skin as well. On the upper left quadrant of the chest and back are a few subcutaneous swellings, freely movable, and varying from the size of a cherry to that of a walnut. There is a larger subcutaneous swelling on the top of the shoulder, where there is also a scar from a previous removal of a portion of this tumour. There are a number of smaller lesions, some of them cutaneous, on the anterior and posterior axillary folds.

On the left arm are a few, mostly small and subcutaneous, lesions. There are several larger lesions in the region of the elbow, particularly on the inner side.

Vascular nævus.

There is a swelling over the lower end of the ulna, which appears to be attached to the bone. The hand is much deformed with a large number of tumours, many of which are cutaneous. There is a large, subcutaneous tumour on the back of the hand, apparently adherent to the tendon sheaths, and there are about five smaller cutaneous and subcutaneous lesions. There are a number of grape-like swellings on the palm and on the backs and fronts of the fingers, especially on the ulnar side of the palm and on the ring and middle fingers.

Report of X-ray examination (Dr. Salmond).—" The soft tissues of the left forearm and hand are studded with soft tissue growths, the majority of which have deposits of some opaque salt.

Bony changes are present at the inner side of the lower end of the humerus, olecranon, lower end of ulna, and first and fourth metacarpals. At the situation of these changes the soft tissue growths are seen, suggesting that the changes are due to pressure or erosion."

Sections show the tumours to be pure angiomata, not nævo-lipomata ; the amount of fibrous tissue in it is very small.

A number of these tumours have been treated in various ways. When the patient was aged 16, five were removed, but some of these have recurred. One has been injected with sodium morrhuate ; it has become a little harder, but there is not much difference in size. Three have been treated with radium needles and have somewhat diminished in size. Two were incised after the application of a tourniquet. The tumours collapsed as soon as the blood was let out, and were thought to be connected with the superficial digital vessels.

Dr. H. SEMON said that he had recently seen, in a baby, a cavernous nævus in the left frontal area. He had intended inserting radium needles into the base of it, but before doing so he thought it advisable to obtain the views of the Radium Institute where many such cases had been cured. Dr. Roy Ward kindly replied that short exposures of a surface applicator " varying from one to two hours were repeated every six or eight weeks." Usually a cure was obtained in from four to six treatments, and he thought radium needles definitely contraindicated in such cases.

Dystrophy of the Nails and Finger-tips.—A. M. H. GRAY, C.B.E., M.D.

F. J., a married woman, aged 52, has been troubled with redness and scaling of the fingers of the right hand for the last four years. The trouble began in 1927 with some cracks on the finger knuckles which later became sore and discharged. This attack subsided, but in 1929 there was a recurrence of the condition ; the nails became discoloured and there was discharge round them. The patient was said to have septic chilblains. For the last two years the hand has been kept tied up and she has scarcely used it.

At the present time the nails of the four fingers of the right hand are dry, brittle, and much broken up. There is also some crusting at the tips of the phalanges, particularly on the middle and ring fingers, suggestive of slight loss of tissue. There is very little change in the thumb nail. The skin of the fingers, and to a certain extent of the right hand, is a little redder than that of the left. The nails were examined for fungus, but none was found. Cultures were proved negative.

The pupils are unequal, the right being slightly larger than the left, and the palpable fissure on the right side is slightly larger than that on the left.

X-ray examination of the cervical region shows rudimentary cervical ribs on both sides, that on the right being considerably larger than that on the left. There is no evidence of any enlargement of the heart or aorta, or of any disease of either lung. A skiagram of the hands shows no pathological change in the bones.

The patient was examined by Dr. F. M. R. Walshe, and he reports with regard to the condition of the hands :—

" I cannot satisfy myself that this is at bottom a nervous symptom-complex. It is true she had cervical ribs, but I cannot see that this has any relation to the condition, and all the ordinary signs and symptoms of rib pressure are absent. The slight myosis and enophthalmos on the left side probably represent an old partial sympathetic lesion, and this can stand in no possible relationship to her finger lesion. It is suggested that she has not a paralytic sympathetic lesion on the left, but an irritative one on the right. I am sure this is pure rationalization to make the signs fit the theory."

The Wassermann reaction is negative.

The eyes have been examined by Sir John Parsons, who reports that the right

pupil is larger than the left, but reacts to light and accommodation. The left pupil dilates irregularly to about 2·5 mm. with cocaine, suggestive of partial paralysis of the left sympathetic. There is no evidence of posterior synechia. The right pupil dilates fully and normally with cocaine. The patient is presbyopic and has been advised to get suitable glasses. The fundi are normal, but there is evidence of arterio-sclerosis causing distension of the veins.

As the patient was slightly hoarse, the throat was examined by Mr. S. A. Beards, but he found nothing abnormal in the upper respiratory passages.

Dr. Kenneth Harris kindly examined the patient's vascular reactions, and reports as follows:—

"The affected hand is colder to the touch than the unaffected. The fingers are blue and the hand is a patchy red and blue. On applying a venous pressure of 70 mm. for three minutes, the cyanosis was much more marked on the right hand and fingers. The reactive hyperæmia after two minutes' occlusion was shorter lasting on the right forearm than on the left. There was only a patchy hyperæmia on the right hand and none at all on the fingers. The left reacted normally.

"With hot water (stinging heat) the vessels of the right hand did not dilate up completely. When the hands were placed in water of 100° F. and pressure of 200 mm. applied to both arms for two minutes, there was no dilatation of the vessels of the right hand.

"With a block of ice on the palms of her hands for five minutes, the hands became cyanosed, but there was no attack of pallor as in Raynaud's disease. After re-warming in hot water there was good dilatation of all the small vessels of the fingers, which became red and hot.

"Immersion of the hands at 15° C., 10° C., and 0° C. for four minutes each produced no attack characteristic of Raynaud's disease.

"Good flares and equal whealing with 1 in 1,000 histamine acid phosphate on each forearm. A wide area of goose skin on the left forearm, but none seen on the right forearm on strong faradic stimulation. With pilocarpine injection, one-sixth of a grain, sweating more on the left side of chest, hand and arm. Sweating equal over the face.

"The pulses on both right and left forearm were found to be equal, using Pachoni's oscillometer."

I brought this case up because I was not clear about the diagnosis. The first question is whether it is a purely skin affection. Is it the result of some septic condition of the hands? Or is the condition due to the fact that she has been keeping the part tied up? Or is it, possibly, a combination of both? I think we can rule out a fungus infection; it does not look like that clinically, and the microscope and cultures proved negative. At first I thought it was a trophic disturbance, but Dr. Walshe is clear that no nerve lesion is present on the affected side. Another question is, is it vascular? It is not thrombo-angeitis, and it appears not to be Raynaud's disease, and, in the absence of pain, it is not erythromelalgia.

Discussion.—Dr. F. PARKES WEBER said he did not think that there was enough evidence to lead one to suppose that this was any kind of tropho-neurosis. The cause should be sought rather in a more purely dermatological direction.

Dr. H. MACCORMAC: It might be a unilateral lupus erythematosus.

Dr. SEMON said he had been puzzled by a case exhibiting similar symmetrical symptoms of the outer three fingers in a woman aged 31. There was the same dry slightly exfoliative tendency, and the slight atrophy of the small pinkish lesions which had troubled the patient for three years because of the subjective sensations of tingling and loss of tactile sensation associated. He took the view that it was a case of lupus erythematosus of unusual type and distribution and prescribed injections of a gold salt. The resulting improvement was very striking and supported the diagnosis suggested.

Dr. S. E. DORE said he had seen a somewhat similar condition in a hysterical woman, who had had several of her nails removed on account of a chronic onychia. The only conclusion he could arrive at was that the condition was artificially produced, and he wondered if that was possible in the present case?

The PRESIDENT, in reply, said that, largely because it was unilateral, he had not thought the condition was lupus erythematosus. He would go into that question. Neither did the possibility of it being an artefact condition occur to him. The hand had been tied up for a long time. He did not see how that type of lesion could be produced artificially.

Lupus Erythematosus.—A. M. H. GRAY, C.B.E., M.D.

The patient, a widow, aged 53, has complained for the last two years of redness and swelling of the face, backs of the hands and forearms, and dryness of the neck and front of the chest.

The eruption began about two years ago while she was convalescing at Brighton after an operation for an abscess in the right groin, the nature of which is not clear. The face and eyes became red and puffy and she attributed this to the cold wind. She had some treatment and the skin gradually became normal.

A year ago she went to California and the eruption on the face relapsed; again she was considerably exposed to the cold wind. Her blood was examined and she was said to be suffering from anæmia. She was given some internal treatment and a calamine lotion for the face and the condition began to improve. She returned to England in December, 1930, and the skin continued to improve until June of the present year, when it relapsed. She has been subject to blueness and numbness of the fingers for the last eighteen months, especially in the cold weather.

At the present time the face appears to be slightly swollen, especially in the region of the eyelids, nose, and naso-labial folds. The skin, when picked up, feels thicker than normal and rather hot to the touch. There is a slight amount of scaling all over the face, but no follicular plugs are present, and the scaling is easily brushed off. There is no sign of atrophy.

On the sides and front of the neck, and over a large "V"-shaped area on the upper part of the chest and over the upper part of the back (the area exposed to light) the skin is red, shiny and rigid, and has numerous opaque white areas and telangiectases scattered over it. The lower edge is ill-defined and fades away gradually into the surrounding skin. There is a certain amount of scaling present.

On the back of each hand and forearm, extending up to about the middle of the latter, is a sharply defined, raised, red patch, with skin thickening and slight scaling. It forms a continuous sheet on the backs of the forearms and wrists, but tends to be broken up on the backs of the hands. It extends on to the dorsum of the thumbs and fingers and is more marked over the proximal and distal phalanges, the middle phalanges being relatively free.

At the roots of the nails telangiectases are visible, and over some of the fingers, particularly the thumb and index finger of the right hand, hyperkeratotic plugs are visible. There are similar patches on the front of both thumbs and on the right little finger; otherwise the palms and fronts of the fingers are free.

The patient has a red, scaly patch over the vaccination scars on the left arm, and some reddish areas which appear to be composed of dilated blood-vessels, but with no skin thickening or scaling, on the lower part of both thighs. On the mucous membrane on the inner aspect of the left cheek is a linear white patch with irregular outline.

In addition to this there is a foliated, pale patch over the upper part of the right scapula, apparently a Vörner's nævus anæmicus.

The blood-count is as follows:—R.B.C. 4,410,000; Hb. 90%; C.I. 1·02; W.B.C. 8,700. *Differential:* Polys. 48%; lymphos. 32·3%; eosinos. 20·5%.

Intradermic tuberculin test, negative.

A section taken from the back of the neck shows only slight changes. The papilla have flattened out so that the dermo-epidermal junction is practically a straight line. The epidermis is otherwise normal. The collagen bundles of the

dermis, especially in the deeper layers, appear to be swollen and the elastic fibres in this area are scanty and broken up. There is no perivascular cellular infiltration and the skin appendages are normal.

It was the condition of the hands, especially above the nail folds, and the hyperkeratotic pitting on the backs of some of the fingers which made me lean to the diagnosis of lupus erythematosus.

Dr. H. W. BARBER said that he regarded this as a definite type of lupus erythematosus; the patch in the mouth and the appearance of the skin behind the nails were conclusive of that diagnosis. He had recently been watching a series of cases in which he found great difficulty in deciding whether he was dealing with true lupus erythematosus or a superficial scaly eczematoid eruption, usually affecting the temples, and often the nose and malar regions. In one case there was definite lupus erythematosus which had left scars on the nose and ears after successful treatment with gold. The patient later came back with this superficial brown scaly eruption along the margins of the forehead, extending into the scalp and down the cheeks. In another case he had been puzzled at first, but diagnosed lupus erythematosus as the patient had definite follicular plugging on the scaly patch on her nose. The eruption cleared up with gold injections, but this year she returned with an eczematoid scaly eruption, but no follicular plugging. He did not think this type of lupus erythematosus was of tuberculous origin; he regarded it as streptococcal. In his second case a relapse definitely followed three injections of a streptococcal vaccine given for colds in which the dominating organism was streptococcus.

Granulosis Rubra Nasi (Jadassohn).—W. N. GOLDSMITH, M.D.

M. S., a boy, aged 7. The nose presents the usual eruption of little, round, red papules together with continuous localized sweating. There is also excessive secretion from the mucous membrane of the nostrils—a running of the nose which necessitates frequent wiping. He also has papular urticaria.

In two cases I have had recently there has been a definite association of rhinorrhœa; the last patient I sent to Mr. J. F. O'Malley had vasomotor rhinorrhœa, and his sister also had vasomotor rhinorrhœa without granulosis rubra. The present patient has continually to wipe his nose without having a cold. No other member of his family affected with granulosis rubra. It must be a disorder of the vasomotor and secretory function of the nose, both skin and mucous membrane. The onset is surprisingly definite. In this case it began three months ago; previously there was no sign of it.

Dr. H. MACCORMAC said he had seen only one example of this condition, and in that the cartilaginous area of the tip of the nose was red and sweated profusely the whole time. In the present case only a small area of skin was involved and sweating was inconspicuous. He doubted if the diagnosis would be accepted.

Smoker's Tongue in a Woman.—H. MACCORMAC, C.B.E., M.D.

This patient is shown because this is the first case I have seen in the post-war period of syphilitic leucoplakia in a woman. Her age is 37 years; the date of infection with syphilis is probably fifteen years ago. She confesses to smoking thirty or more cigarettes a day and has done so for about twelve years.

The superficial type of the leucoplakia is present on the dorsal surface of the tongue on the anterior half, and also on the buccal mucosa. The Wassermann reaction is positive.

This disease is comparatively common in men who have had syphilis and are pipe smokers. Many of the cancers of the tongue develop upon a leucoplakia of this kind, and it is possible that this type of malignant disease will in future be met with in women as well as men.

Discussion.—The PRESIDENT asked whether Dr. MacCormac considered that this type of tongue was always the result of a combination of the two factors syphilis and smoking. His own idea had been that it could be caused by syphilis alone; he had seen a worse tongue in a woman who had not smoked at all. With regard to the so-called "smokers' patches" in the buccal mucous membrane, he thought these could occur independently of syphilis.

Dr. H. MACCORMAC (in reply) said he thought this condition was a product of the two factors he had mentioned, and that view was shared by Darier and others. Leucoplakia was so common in male syphilitics that he considered it almost as useful as the Wassermann test in old-standing disease.

Chrysanthemum Dermatitis.—H. MACCORMAC, C.B.E., M.D.

The patient, a woman aged 26 years, first observed an eruption on the face 12 years ago; this has recurred annually, with the exception of one year when she changed her occupation from that of a country domestic to that of a shop assistant in a town. The hands have never been affected. When first seen at the out-patient department her face was markedly swollen and œdematous. The appearance of the eruption and the history pointed to some external agent, probably chrysanthemums, with which it was found she had been in contact. She was admitted into hospital, and when the condition had subsided, chrysanthemum petals were rubbed into the skin on one side of the face, and chrysanthemum leaves on the other. The result was a return of the eruption in acute form on the next day. Later, some of the actual plants from the house in which she was employed were obtained and these were applied to the scapular region on the right side with a pronounced flare up on the face and slight dermatitis of the shoulder.

Examples of chrysanthemum dermatitis are rare. E. Hoffman [1] reported one in 1904, and recently another case has been recorded by G. S. Nightingale [2] in a market gardener. One other case has come under my observation in a hospital nurse who every autumn for several years developed a rash about her mouth and nose. It was ascertained that she was in the habit of smelling chrysanthemums and when this was discontinued the eruption disappeared. She was unwilling to allow a test of the effects of the plant on her face, but on the arms where the leaves and flowers were applied the result was negative. The sensitiveness of the skin would therefore appear to have been local.

Graduated injections of the essential oils which exist in the leaves in proportions varying from 0·01 to 0·1% were first considered as a method of desensitizing the patient in this case. Later a simpler method was devised, viz., rubbing the plant into the skin through measured areas cut in scale in stiff paper. An increasing dose of the antigen can thus be accurately given. For this purpose the thigh has been selected, where the reaction has not been unduly severe.

References.—[1] E. HOFFMAN: *Muench. med. Woch.*, 1904, li, 1966. [2] G. S. NIGHTINGALE, *Lancet*, 1931, (i), 1132.

THE PRESIDENT said he had himself seen two instances of chrysanthemum dermatitis. Both were in florists, and the patients themselves knew what was responsible for the condition.

CORRIGENDUM.

Widespread Superficial Lupus Erythematosus.—LOUIS FORMAN, M.D., for H. W. BARBER, M.B. *Proceedings*, 1931, xxv, 218 (Sect. Derm. 8).

Lines 27 to 31 should read as follows:—

"In 25 cases of chronic fixed lupus erythematosus, 42% gave a strong positive

reaction, and a further 18% a positive reaction, to hæmolytic streptococcal vaccine injected intradermally.

16% gave a strong positive reaction, and a further 20% a positive reaction, to tuberculin.

In 13 cases of superficial lupus erythematosus, 70% gave a strong positive reaction, and a further 23% a positive reaction, to hæmolytic streptococcal vaccine. 20% gave a strong positive reaction to tuberculin, and a further 30% gave a positive reaction, to tuberculin."

Clinical Section.

[*December* 11, 1931.]

Sarcoma of Right Orbit: After Operation.—CECIL P. G. WAKELEY, F.R.C.S. (President).

This patient, S. J., aged 17, was shown before this Section in February, 1931,[1] after radium treatment had been used (fig. 1). In March, 1931, the right eye became more prominent and enucleation was decided upon.

FIG. 1.—Condition of eye before removal of orbital contents.

Operation, 25.3.31.—The eye and all the orbital contents were removed and also the orbital plate of the frontal bone. The raw area left by this operation was allowed to granulate and the base of the orbital cavity was skin-grafted, 27.6.31.

1 *Proceedings*, 1931, xxiv, 687 (Clin. Sect. 63).

FIG. 2.—Condition after removal of orbital contents.

FIG. 3.—Patient with spectacles and eye painted on metal plaque.

The graft took very well and the patient was discharged 9.7.31 (fig. 2). In October, 1931, a metal plaque on which an eye had been painted by my colleague Mr. Arthur Edmunds was fitted to a spectacle frame, and the patient is just beginning to wear this (fig. 3).

Osteoma of Neck of Femur.—CECIL P. G. WAKELEY, F.R.C.S.

Patient, male, aged 35, labourer. Family history negative. Complaining of aching pain in left hip and lumbar region, for two years. Increasing difficulty in walking owing to "increase in length of left leg." No history of trauma. Gaining weight.

Left hip.—Abducted; adduction limited; flexion to 90° only; no fixed flexion. Left leg ¾ in. apparent lengthening. No true shortening. Left gluteal fold absent. An indefinite swelling can be felt, on deep palpation over the left buttock. Skiagram shows a large osteoma, growing from the neck of the left femur.

I think that operation should be undertaken as the tumour is pressing on the rim of the acetabulum and this causes limitation of movement and pain when the man attempts to walk.

Skiagram (Dr. Graham Hodgson) showing the large osteoma of the neck of the femur.

Postscript.—Operation, 16.12.31. The osteoma was exposed through a posterior incision; it was found to arise outside the joint, just above the lesser trochanter.

It was completely removed, and the raw surface on the femur was rubbed over with Horsley's wax. The operation was quite a simple procedure.

Bilateral Snapping Knee.—A. ROCYN JONES, F.R.C.S.

A. V., a girl aged 16, complained in 1929 of a curious sound in each knee during movement; this had been present all her life, but had become worse. The left knee, in particular, had been painful lately and had let her down. On examination

each knee exhibited a loud, grating sound when the joint was reaching full extension from a position of flexion. The sound was accompanied by a jerking movement of the knee, as though some body momentarily impeded its smooth action. This body was distinctly palpable on the outer side.

Operation (left knee).—The joint was explored on the outer side and the external cartilage was found to form a complete disc. The cartilage was completely removed. The symptoms have entirely disappeared from the left knee; the joint has a full range of stable movement. The right knee continues to exhibit the same symptoms as those in the left knee before operation, and it is presumed that the same pathological condition exists in the right knee. The complete disc is a congenital anomaly and is a common cause of so-called "snapping knee." The right knee is unstable and the patient desires an operation on this joint.

The PRESIDENT said that the right knee-joint should certainly be operated upon, as Mr. Rocyn Jones had obtained such an excellent result on the left side. The snapping condition, which would persist if no operation were performed, would eventually lead to some chronic synovitis of the knee-joint.

Gaucher's Disease: Splenectomy.—BERNARD MYERS, C.M.G., M.D.

Jean W., admitted to Royal Waterloo Hospital last September, aged 2 years and 9 months, suffering from distinct enlargement of the abdomen, and from anæmia. Looked obviously ill; never smiled; had a pathetic and serious expression. Skin all over body was of slightly yellowish tinge. Chest and limbs looked small in comparison with abdomen. Appetite fairly good but varied; had always been constipated. The motions were on the pale side and never dark. As a rule she slept well, but was sometimes wakeful.

She walked when eighteen months old. Although she rarely speaks in hospital, her mother states that she talks a great deal at home.

On examination.—Nothing abnormal noted in heart and lungs. The great prominence of the abdomen was due to the spleen, which reached down to the pubes and just across the middle line, and to the liver, which extended three finger-breadths below the costal margin. Both organs were smooth and the edges could be felt; neither was tender. No fluid present. There was a fair-sized umbilical hernia.

A few small glands palpable in anterior triangle of the neck. Thymus appeared to be normal in size. Nutrition of skin and muscles was poor. There were no pingueculæ.

During the last three months there had been three attacks of epistaxis; the last occurred two weeks previously and was rather severe, being followed by the vomiting of an appreciable quantity of blood. Urine normal.

Patient was a full-time child; birth-weight 6¼ lb. Apparently nothing abnormal was noted until she was three months old, when the mother observed some enlargement on the left side of the abdomen "with something moving inside when the child was turned over." At a Welfare Centre nothing was mentioned except that the child was thin. The abdomen slowly continued to enlarge until the admission to hospital.

Previous illnesses: Tonsillitis at a year and 4 months, and a few months later broncho-pneumonia.

Family history.—Mother a little anæmic but otherwise well. Father, who is a police constable, is a very healthy individual. There is one other child, eighteen months old, who enjoys perfect health. There is no similar case to the patient's in the family.

Examination of blood (F. A. Knott).—R.B.C. 1,350,000; Hb. 19%; C.I. 0·7; W.B.C. 2,200. During the count of 280 cells two myelocytes and a number of young polymorphonuclears were seen, which, Dr. Knott thought, did not necessarily indicate a leukæmic process. The red cells were pale, irregular in shape, and often diffusely basophilic; no nucleated red cells. Clotting time, normal; bleeding time, six minutes; platelets 75,000 per c.mm.

Differential leucocyte count.—Polys. 44%; eosinos. 2%; basos. 1%; large hyalines 14%; lymphos. 39%.

Van den Bergh reaction negative (direct and indirect). Wassermann reaction negative. Fragility of reds, normal. Slight hæmolysis in 0·45% saline; none in 0·475%.

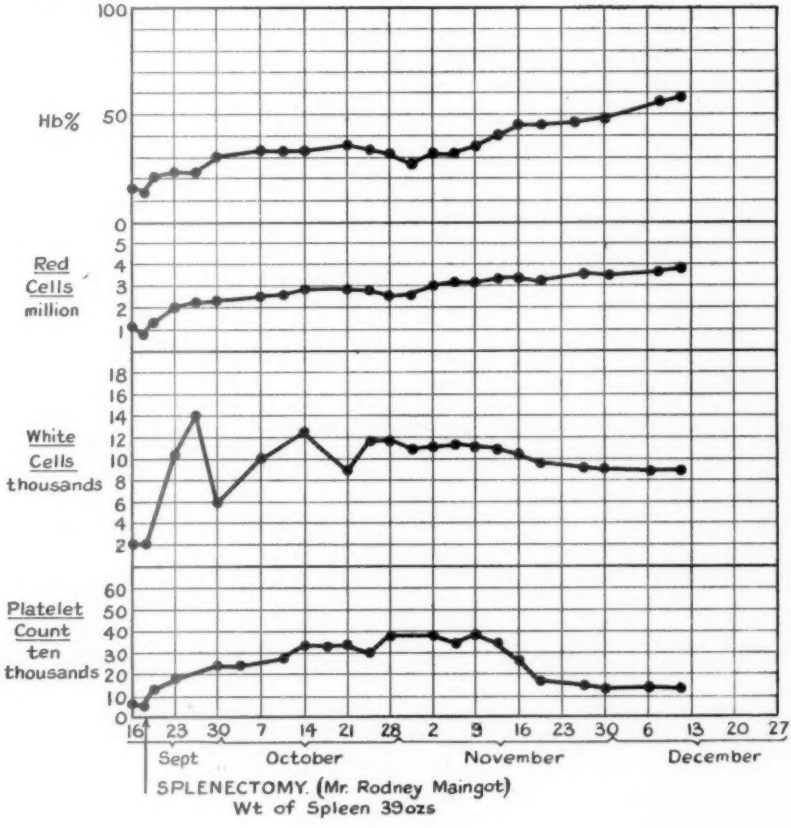
Urine: No albumin, sugar or bile; urobilin, no excess. Deposit was purely mucoid; no abnormalities. Cultures quite normal.

Examination of stools showed slight excess of split fat (fatty acid); no unsplit fat; no undigested muscle or starch. Cultures normal; *Bacillus coli communis* and enterococci only occur. Large amounts of stercobilin present. No evidence of blood, pus, etc.

In a child of this age with the history, the enlarged spleen and liver, the blood picture, etc., and Banti's disease, Hodgkin's disease, tropical diseases, amyloid disease, leukæmia, pernicious anæmia, acholuric jaundice, tuberculosis, syphilis, etc., being negatived, the question of making a splenic puncture to prove the probable diagnosis of Gaucher's disease was contemplated, but as the hæmoglobin went quickly to 16%, and the child's condition was most serious, I asked Mr. Rodney Maingot to perform a splenectomy at once, as the epistaxis might have recurred. This was carried out on September 17.

The child made an exceedingly good recovery, notwithstanding an attack of lobar pneumonia on the third day after operation. The red cells soon rose to 2,000,000, and the hæmoglobin to 30%. Platelets were now plentiful, being about 200,000. Normoblasts were fairly numerous, but no myelocytes were seen.

Blood counts:



The weight before operation was 1st 9 lb. 4 oz.; afterwards it fell to 1 st. 5 lb. 12 oz., and is now 1 st. 7 lb. 10 oz.

Report on spleen.—Weight when received at laboratory shortly after removal was 39 ounces.

The surface of the spleen is smooth and the capsule not specially thickened. A few small old infarcts are seen but no recent ones. No major adhesions had been formed.

On section the organ appears rather tough and contains extensive zones in which the normal colour is replaced by a slaty-pink.

The most striking feature of the microscopical sections is the replacement of large areas of the pulp by large relatively solid masses of cells of the Gaucher type. Some of these cells exceed 30μ in diameter and are multinuclear. They stain very faintly and their protoplasm has often a decidedly reticulate appearance. They do not appear to stain with either Sudan III or osmic acid. It has not been possible to examine them by polarized light.

Apart from the solid masses of cells, a few free groups are seen within the sinuses.

The spleen itself is congested. The Malpighian bodies are apparently not hypertrophic. [F. A. Knott.]

Since recovery from pneumonia the patient has taken 1 oz. of minced cooked liver morning and afternoon, and a mixture containing iron and ammonium citrate and liquor arsenicalis.

X-ray examination has not, so far, shown any bony changes. One case of spontaneous fracture of femur has been noted in a child with Gaucher's disease.

Graham and Blacklock are of opinion that the disease is a reaction of the cells of the reticulo-endothelial system to some metabolic error in lipoid metabolism and believe that the Gaucher cells contain a substance of a fatty nature. They have noted transition stages between reticular cells and Gaucher cells in the Malpighian bodies of the spleen and lymphatic glands.

Dr. F. PARKES WEBER said that in a disease so widely distributed over the body as Gaucher's disease, it was a question whether it was worth while excising the spleen, which was a relatively small portion of the whole disease. Splenectomy was perhaps justified when there was evidence of "hypersplenism," that is to say, of harmful functional over-activity of the spleen. The relatively good result, at all events for the time, of splenectomy in Dr. Myers's case confirmed the view that there was "hypersplenism" in some cases of Gaucher's disease.

Lymphadenoma with Intermittent Pyrexia (Pel-Ebstein Type).—TERENCE EAST, D.M.

The patient is a boy, aged 13 years. Enlarged glands first noticed five months ago. Pyrexial attacks before admission to hospital. During the last month three attacks have been observed. The pyrexial phase lasts about a week (see temperature chart). During the attack the glands become much enlarged, tender and hot, and the skin over them is red; the spleen increases in size. Between the attacks the glands are slightly enlarged on both sides of the neck, and the spleen can just be felt.

Pain in the back during the pyrexial phase suggests that the lumbar glands are involved, and in the skiagram the bronchial glands appear to be large.

When first under observation the epitrochlear glands could be felt, and there were two large glands in the right axilla. The glands in the groin are not large.

Blood count.—Between attacks: R.B.C. 110%; Hb. 102%; W.B.C. 9,200; polys. 73·5%; eosinos. 5·0%; lymphos. 21·5%; (on another occasion): W.B.C. 4,400; polys. 50%; eosinos. 6·8%; lymphos. 41·2%; hyals. 2·0%.

During the attack: W.B.C. 6,400; polys. 82·0%; eosinos. 9·5%; lymphos. 8·5%.

Wassermann reaction negative. Mantoux test positive at dilution of 1 in 10,000.

The last attack was more severe than the preceding ones.

Raynaud's Disease, Sclerodermia, Telangiectases, Paroxysmal Eye Troubles and Paralysis Agitans.—E. STOLKIND, M.D.

Female, aged 49, came with complaints of fingers, toes, eyes and telangiectases on the face, etc., and of stiffness and tremor in the right side. Patient is of a healthy family. Mother was healthy until the age of 61, when all her teeth were taken out. The patient was an anæmic child and easily tired. At the age of 12 various parts of her body were burned and there are scars. Until the age of 18 there was nothing wrong with her fingers or toes, but since that time she occasionally had "festering" of her fingers. At 21, the right middle finger used to go white and numb. Later, in cold weather, the fingers and toes became purple, cyanotic, numb as far as the wrists and ankles, and even painful. Usually she would then put her hands in warm water or sit near the fire. In from five to twenty minutes the attacks, which usually occurred in the morning just as she got out of bed, would pass off. If she did not warm her hands and feet the attack continued for many hours and she was unable to even move her fingers or walk. During these attacks the hands and feet (especially soles) perspired a great deal. At the age of 31, in addition to these attacks, she began to notice a slight glossiness of the skin of her face.

In 1917 Dr. F. Parkes Weber showed her [1] at a meeting of the Section.

"No bony changes could be detected in the hands and feet by Roentgen rays. There was some shiny skin over the upper part of the sternum and below the clavicles, indicating the commencement of generalized sclerodermia and facial skin was likewise already slightly involved (tenseness and glossiness)."

Since 1917 the hands and feet have become more pronouncedly affected. The fingers have been more often swollen and stiff and the skin on them and the toes has peeled. Some of the fingers are colder than others. They are all rather thick and almost all had some scars. All the nails are short, wrinkled and hardened.

The skin of the hands, mainly of the fingers which are scarred, is rigid. There is little power of extension of the fingers and still less of flexion. The toes are bluish-white, the skin is stiff. There was a small ulcer in the ear and tuberculosis (surgical).

X-ray examination (Dr. Martin Berry): The tips of the terminal phalanges of the left thumb, index and middle finger and the right middle finger have been absorbed. Each little finger is deformed but shows no evidence of bone disease. Each foot shows a bunion and possibly slight general bony atrophy.

The skin of the face and over the sternum is rigid and shiny.

On the face, exposed part of the sternum and chest, and to a less degree on the neck, there are patches of shiny telangiectases from 1 to 15 mm. long and from 1 to 5 mm. wide.

The face is sometimes pale, but at others is very red and hot. The nose becomes cold suddenly. If the hands and fingers are dipped in cold water, they become cyanotic. Lately, there have been attacks of inability to see, lasting from ten to twenty minutes. Nothing abnormal could be discovered in the eyes. Pulse, 90. Blood-pressure, 132/85. Wassermann reaction, negative. Blood, almost normal. The menstrual discharge consisted of a few stains and menstruation lasted only a few hours, occurring every three or four weeks since she was 18. It ceased ten years ago. For the last five years signs of Parkinsonian disease have gradually appeared, beginning with dribbling of saliva and then tremor and rigidity of the right side.

There is now the so-called "Parkinsonian mask-like face" with rigidity of the muscles and symptoms of vasomoter, sensory and secretory disturbances—attacks of perspiration, rushes of blood to the head, increased salivation, polyuria, etc. Speech is slow and monotonous and lately patient has begun to stammer.

Protein therapy, including injections of angioxyl, was of no use.

1 *Proc. Roy. Soc. Med.*, 1917, x (Clin. Sect., 16).

This is a rare case. For the last 15 years the sclerodermia has not increased but the condition of the toes and hands, especially the fingers, has altered considerably. In addition there are now telangiectases, visual disturbances and paralysis agitans. It is difficult in this case to explain with any certainty the kind of association of Raynaud's disease, sclerodermia, etc., with paralysis agitans. In all probability internal secretion (ovarian, etc.), the vegetative nervous system, and lesions in the arteries are important factors.

Dr. PARKES WEBER said that he had often expressed the view that angiospastic symptoms like Raynaud's disease (dead fingers and acro-asphyxia) were so frequently associated with sclerodermia of the sclerodactylia type that they should be regarded as part of the symptomatology of the disease. Lately, however, Sir Thomas Lewis and Dr. E. M. Landis (*Heart*, 1931, xv, p. 329) had suggested that the angiospastic symptoms might be a causative factor of the sclerodermatous change. He, Dr. Weber, thought that the Parkinsonism was not causally related to the other features in this case; it was hardly ever met with in association with sclerodermia.

Diverticulum of the Duodenum.—D. C. HARE, C.B.E., M.D.

Mrs. C. Z., aged 44, first seen in March, 1931, suffering from "indigestion" of about twelve months' duration. She complained of flatulence, with feelings of hunger and internal rumblings and of occasional pain in the right hypochondrium about an hour and a half after taking food; she had recently felt nausea but

Diverticulum of duodenum.

had never vomited. She had lost about a stone in weight. The bowels were constipated and she suffered from uterine prolapse. She had always been very healthy and had not been subject to indigestion previously. At the present time she is almost free from all these symptoms, her appetite is very good and she has gained weight. She is still troubled with borborygmi, and if she is tired and takes a heavy meal it is followed by epigastric discomfort. On physical examination nothing abnormal can be palpated. The abdominal wall is very thin and soft, there is divarication of the recti and the normal peristaltic movements are often visible.

X-ray examinations by Dr. Eva White show a large diverticulum, about the size of a tangerine orange, arising at the junction of the second and third parts of the duodenum and lying on the outer side of the curve. It is quite mobile and varies greatly in position; it is not tender when palpated directly under the screen. There is no enlargement of the duodenum and only a slight tendency to retention of the meal in the gut itself. The stomach is low in the erect position and shows a little retention at four hours. There is no diverticulosis of the colon.

The fractional test-meal shows a normal resting juice, a normal acid curve and slight delay in the emptying rate.

The Wassermann and Sigma reactions are negative.

Remarks.—A considerable literature on the subject of diverticula of the duodenum has been published in the last few years though the condition is not very common. There are probably many cases in which symptoms are entirely absent and it is only in those individuals in whom it is associated with digestive disturbances and who are examined with an opaque meal that the diagnosis is made; diagnosis by clinical symptoms and signs appear to be impossible.

Spriggs and Marxer [1] have reported on thirty-eight cases, twenty of whom had no symptoms; of those with symptoms, thirteen were cured by medical treatment. In the present case the early symptoms passed off in a few weeks without specific treatment and have not recurred. Operation is called for only when complications are present, as by involvement of neighbouring structures or the presence of a calculus in the sac, as in a recent case published by Scott [2]. Interesting discussions on the causation are to be found in papers by Gask [3], Odgers [4], and Hahn [5].

REFERENCES.

[1] Spriggs, E. I., and Marxer, *Quart. Journ. Med.*, 1925, xix, 1. [2] Scott, S. G., *Brit. Med. Journ.*, 1931 (i), 346. [3] Gask, G. E., *St. Bartholomew's Hosp. Rep.*, 1929, lii, 122. [4] Odgers, P. N. B., *Brit. Journ. Surg.*, 1930, xvii, 592. [5] Hahn, O., *Klin. Wochenschr.*, 1930, ix, 1922.

The President said that in his experience duodenal diverticula usually occurred on the concave inner surface of the second part of the duodenum, in the neighbourhood of the papilla of Vater. He was also very emphatic that duodenal diverticula were usually associated with diverticulosis or diverticulitis of the colon.

In this case, the duodenal diverticulum was in an uncommon situation, and there was no associated diverticulosis of the colon. In his opinion, an isolated diverticulum of the duodenum rarely gave rise to any symptoms by itself.

Aneurysm of Aorta with Bronchiectasis.—B. T. Parsons-Smith, M.D.

W. H. M., male, aged 64.

Subjective symptoms.—Physical fatigue and breathlessness on exertion during the past two years, cough with mucopurulent expectoration and, recently, effort-pain in the right arm and shoulder.

Physical signs.—Heart enlarged to left, apex impulse in fifth space 4 in. from the mid-line; area of dullness increased at the base extending 2½ in. to right of mid-line in second and third spaces; rhythm regular except for occasional premature contractions; systolic and diastolic murmurs, also thrill in aortic region; systolic murmur at apex; pulse 84, an occasional intermission; vessels thickened and tortuous; blood-pressure 170/105.

Electrocardiogram.—Curves indicative of myocardial degeneration (low voltage T-waves) and left ventricular preponderance; lungs—impaired percussion note, deficient air entry and scattered râles at right base.

X-ray examination.—Large aneurysm of ascending aortic stem which projects forwards and to right into lung field; hypertrophy of left ventricle; extensive area of mottled opacity at right lung base and diminished excursion of right lobe of diaphragm.

Congenital Cerebellar Ataxia with Auditory Aphasia.—B. SCHLESINGER, M.D.

S. W., female, aged 3 years and 9 months.

History.—Has never spoken. Began to walk at age of 10 months, but gait was noticed to be peculiar. Very nervous and "jumpy." No history of fits. Normal birth. No past illnesses.

Family history.—One other child apparently normal, died from pneumonia. No history of similar condition in any other member of the family.

On examination.—Wide gait, coarse nystagmus. No definite Rombergism. Reflexes: Right knee-jerk absent, left very weak; ankle-jerks absent; abdomina reflexes all present; triceps, biceps, and supinator reflexes present on both sides; plantar reflexes both flexor. No definite alteration in sensation to pain or touch. Discs appear to be normal. Wassermann reaction negative.

Lymphadenoma with Involvement of the Spinal Cord.—REGINALD LIGHTWOOD, M.D. (by permission of Dr. HUGH THURSFIELD).

History.—A. C., aged 10, one of a healthy family of four children, was found over three years ago to have an enlarged spleen. "Splenic anæmia" was diagnosed. For the last eighteen months the boy has been worried with breathlessness and cough.

Hospital records.—He was admitted to the Hospital for Sick Children under Dr. Hugh Thursfield in June, 1931.

On examination.—Pale and thin; fingers and toes clubbed. Night sweats. Spleen enlarged four fingers-breadths, firm and nodular. Liver margin found three fingers-breadths below costal border. Mass of glands in mediastinum (confirmed by radiogram); enlarged lymphatic glands in neck, axillæ and right groin. Central nervous system normal. Mantoux (1 in 1,000 O.T.) negative.

Blood.—R.B.C. 5,000,000; Hb. 55%; C.I. 0·5; W.B.C. 12,500. *Differential*: Polys. 5,750 per c.mm. (46%); lymphos. 6,250 per c.mm. (50%); lymphoblasts 125 per c.mm., (1%): monos. 250 per c.mm. (2%); eosinos. 125 per c.mm. (1%).

Biopsy (cervical gland).—An enlarged gland undergoing fibrosis. The normal structure is lost and the appearances are those of lymphadenoma. There are numerous eosinophils and some giant cells and areas of degeneration.

Treatment.—Two courses of intravenous antimony tartrate were given. This seemed to have no effect except for diminution in the sweating. The second course was interrupted because melæna occurred.

August, 1931.—Transferred to Tadworth Branch Hospital, where Dr. Ritchie noted: "Pale, poorly nourished, slightly cyanosed, clubbing. Physical examination revealed the same condition as above, except that the right knee-jerk was more easily obtained than the left; abdominal reflexes present; no ankle clonus; no weakness; plantar responses flexor."

September 8, 1931.—Weakness of the legs first noticed. Left knee-jerk more sluggish than before. Plantar responses extensor and double ankle clonus present.

October 22, 1931.—A vesicular eruption, diagnosed as herpes zoster, came out on both sides of the trunk (level not stated). Four days later this was fading.

Œdema of the feet was recorded from time to time, but albumin was not found in the urine. The temperature charts show an intermitting fever of the Pel-Ebstein type.

November 20, 1931.—Readmitted to Hospital for Sick Children for X-ray therapy.

Present condition (*December* 4, 1931).—Pale, thin, cyanosed, orthopnœic. Clubbing of fingers and toes; lymphatic glands enlarged in neck, axillæ and right groin and over upper part of thorax. Œdema of ankles, left more than right. Œdema of scrotum.

Thorax: Right parasternal bulging. On percussion a globular area of dullness is found in the anterior part of the mediastinum behind the sternum and the anterior ends of the ribs. This is due to a mass of glands which can be felt rising up into the supra-sternal notch. Cavernous breathing and whispering pectoriloquy is heard over the dull area. Posteriorly there is a positive d'Espine's sign (D.5). Numerous sibilant râles are heard on both sides.

Abdomen: Enlarged; a net-work of veins is seen in the anterior abdominal wall; ? shifting dullness. Liver enlarged three fingers-breadths. Spleen irregular and nodular and extends into left iliac region.

Central nervous system: Weakness of legs, especially left; diminution of sensation in legs, especially below knees.

Reflexes.

	Right	Left
Knee-jerks ...	Present ...	Absent
Ankle-jerks ...	Increased ...	Present
Ankle clonus ...	Present ...	Present
Babinski ...	Present ...	Present
Cremasteric ...	Brisk ...	Diminished
Abdominals ...	? absent ...	? absent

Blood.—R.B.C. 3,375,000; Hb. 40%; C.I. 0·6; W.B.C. 5,620. *Differential*: Polys. 4,327 per c.mm. (77%); lymphos. 900 per c.mm. (15%); monos. 337 per c.mm. (6%); eosinos. 56 per c.mm. (1%); myelos. 112 per c.mm.

Literature.—Compression paraplegia in lymphadenoma has been recognized for many years and the late Sir William Osler mentioned it in 1923. F. Parkes Weber described a case[1] and later summarized the cases published up to the year 1925.[2] In 1927 C. F. T. East and R. C. Lightwood published a case in which there was paraplegia, with involvement of the upper limbs as well, and they discussed the morbid anatomy and mechanism of spinal involvement in Hodgkin's disease.[3] More recently Eugénis (1929) collected sixty cases of involvement of the nervous system, and in 1930 Schaeffer and Horowitz again reviewed the subject and described two additional cases. F. G. Poynton and K. E. Harris added another in 1930.[4]

Erythromelalgia-like Symptoms with High Blood-pressure.—F. PARKES WEBER, M.D.

The patient, J. R., aged 45, Polish Hebrew, has for the last one and a half years been troubled with pain and lividity in the toes of both feet, which commenced gradually in the little toe of the right foot. Though pulsation is unusually marked (almost excessive) in the arteria dorsalis pedis of both feet, slight superficial "acro-necrosis" has nevertheless developed at the tips of some of the toes. No history of excess in tobacco or alcohol. Brachial blood-pressure: 200/140 mm. Hg. Slight enlargement of the left ventricle of the heart. Nothing abnormal in regard to the urine and blood-count. Negative Wassermann and Meinicke

1 Weber, F. Parkes, *Quart. Journ. Med.* 1923, xvii, 1.
2 Id., *International Clinics*, 1926, i, 126.
3 East, C. F. T., and Lightwood, R. C., *Lancet*, 1927, ccxiii, 807.
4 Poynton, F. G., and Harris, K. E., *Lancet*, 1930, ccxix, 903.

reactions. Blood (serum) cholesterol; 200 mgm. %. No X-ray evidence of calcified arteries in lower limbs.

The case seems to lie halfway between Weir-Mitchell's erythromelalgia and angio-spasm (Raynaud's syndrome) of the small arteries supplying the toes, but I expect that thrombosis has occurred in some of these arteries. The rather excessive pulsation in the dorsal artery of both feet is rather against the case being one of true thrombo-angiitis obliterans (Buerger's disease).

Osteoma of Ilium.—H. L. C. WOOD, F.R.C.S.

Patient, a woman aged 28, complains of a swelling in the right side of the abdomen of four years' duration and increasing in size. Lately it has begun to ache. On examination, a bony swelling can be felt in the right iliac fossa, firmly attached to the ilium. Rectal examination negative.

A skiagram shows a large osteoma growing apparently from the right ilium. This woman's sister had a cervical rib.

Sarcoma of Leg.—S. I. LEVY, F.R.C.S.

V. V., aged 22. Swelling of lower end of left fibula was noticed two years ago. Painless at first, but now has night pain. No history of trauma.

Attended London hospital twelve months ago. Wassermann reaction negative. Treated with potassium iodide which, according to patient, made the swelling smaller.

Two small nodules appeared on antero-lateral aspect of swelling four months ago. Skiagram of leg taken then showed osteo-periostitis. Wassermann reaction again negative.

When patient was seen by me three weeks ago there was diffuse swelling of the lower third of the left fibula, and there were two nodules apparently adherent to the fibula. Night pain present. Wassermann reaction negative. Skiagram of distal third of left fibula shows thickening of bone, obliteration of canal, irregular inner and outer borders. The appearances suggest osteo-periostitis.

Under local anæsthesia I excised one of the nodules. It was adherent to the bone. *Pathological report*:—

"The nodule is almost completely surrounded by dense fibrous tissue from which run septa into the growth, which is composed of a network of fine fibrous tissue, surrounding masses of round cells which are supplied with blood by many vessels, some of which are thin endothelial-lined sinuses. Appearances are those of a neoplasm of a round-celled sarcomatous type."

Carcinoma of the Male Breast.—HUGH S. STANNUS, M.D.

Patient, male, aged 51, a French chef. The growth in the left breast was discovered on routine examination upon admission to hospital for a rheumatoid affection. Except for one small hard gland high up in the axilla of the same side there were no signs of metastatic deposits. The patient complains of no symptoms in reference to the neoplasm and "thinks" it began between four and five years ago.

Giant Papilloma of the Face.—RODNEY MAINGOT, F.R.C.S.

This case of tumour of the face is remarkable not only for the size and appearance of the tumour, but also for the mentality of the patient (M. M. T., aged 48 years),

who allowed such a foul and unsightly growth to persist and slowly advance without seeking medical advice.

The growth began five years ago as a small wart on the right side of the nose. It spread very slowly until the end of the summer of 1930 when it was about the size of a sixpenny piece. After Christmas, 1930, it extended more rapidly, and the patient was treated by quack remedies through correspondence. Since June, 1931, it has grown very quickly, until it now obliterates the nose and a portion of each cheek, and is encroaching on the eyes, obscuring the field of vision. It was owing to this latter development that she sought medical advice early in December, 1931.

When I examined her, the growth was occupying a central position in the face completely obliterating the nose, and extending laterally on to the cheeks, infiltrating the upper lip, and eroding the inner canthus of each eye. The foul-smelling mass

Giant papilloma of face.

was exuding pus from its numerous fissures and necrotic areas, was very soft, friable, and decomposing in the centre, and at the periphery was rolled over, hard and purplish. The edge had all the appearance of a rapidly-growing epitheliomatous ulcer; large eczematous patches occupied the malar regions, and septic, radiating cracks led to the margins of the tumour.

On transillumination the left antrum was opaque. An extraordinary feature of this case is that, although the growth had existed for over five years, was septic and rapidly growing, no glands could be palpated in the neck.

I considered that the condition was beyond all surgical relief, and that both radium and X-ray treatment were inadvisable.

The photograph of the patient—taken in December, 1931—depicts quite clearly the main features of this enormous papillomatous growth.

Intermittent Claudication in a Woman.—F. PARKES WEBER, M.D.

The patient, C. D., aged 63 years, is a Polish Jewish, slightly corpulent woman, who for the last fourteen years has had intermittent claudication in both lower limbs, but chiefly the right one. She has likewise sometimes had pains in the chest on walking, suggesting slight angina pectoris. Her feet have the dusky and often pallid features as in thrombo-angiitis obliterans; the cyanotic discoloration is especially of the right foot. No pulsation felt in either arteria dorsalis pedis. Brachial blood-pressure (right side): 200/100 mm. Hg; (left side), 230/130 mm. Hg. The left radial pulse is slightly larger than the right. Negative Wassermann and Meinicke reactions. No history of alcoholism or tobacco. Heart (radiogram) slightly enlarged to left. Urine, free from albumin, sugar and excess of urobilinogen. No X-ray evidence of calcified arteries in lower limbs. Nothing abnormal in the blood-count. Dr. Weber thinks that the intermittent claudication in this case has been due to arterial atheroma and not to thrombo-angiitis obliterans. A point somewhat supporting this view is the high blood (serum) cholesterol (December 5): 248 mgm. per 100 c.c. Dr. Weber has never seen a true case of thrombo-angiitis obliterans in a woman.

Section for the Study of Disease in Children.

[*November* 27, 1931.]

Massive (? Active) Pulmonary Collapse following Pneumonia.—LEONARD FINDLAY, M.D.

A. D., a boy, aged 7 years, whose previous health is without interest save that at the age of 7 weeks he had been operated upon for congenital hypertrophic pyloric stenosis, was admitted to East London Hospital for Children with the story that two weeks previously he had developed a cough and was fevered. One week later he had experienced substernal pain which lasted for a day or two, and during the two days immediately preceding admission he had a moderately profuse muco-purulent expectoration.

On admission to hospital the temperature was normal, as also were the pulse and respiration rates. Examination of the chest revealed dense dullness at the left base behind below the angle of the scapula, with intensely tubular, almost amphoric,

FIG. 1.—Showing the dense triangular shadow due to collapse of lower lobe of left lung.

breathing and whispered pectoriloquy and occasional sub-crepitant râle. There was also evidence of the heart being either enlarged or displaced to the left, the apex beat being situated in 5th left interspace 3 in. from the middle line and the left border of the area of cardiac dullness 3¼ in. from the mid-line; the heart's sounds were soft but unaccompanied by murmur. With the exception of a carious tooth and a periodontal abscess nothing else abnormal was detected on physical examination.

A diagnosis of lobar pneumonia with delayed resolution was made, but X-ray examination only revealed a questionable patchy consolidation in the neighbourhood of the apex of the left ventricle. There was present, however, in a marked degree, the triangular shadow overlying the cardiac shadow which has been variously ascribed to a mediastinal pleurisy [1], a fibrosis of the lung with bronchiectasis [2], and to a partial collapse of the lung [3] (fig. 1). This shadow is uniformly dense, is

triangular in shape, commences in the middle line, has its base on the diaphragm and the hypotenuse, describing a concave curve, runs from about the level of the bifurcation of the trachea to the centre of the left dome of the diaphragm. The same appearance may be present on the right side.

In this patient lipiodol injection failed to reveal any evidence of bronchiectasis. On the assumption that there might be a partial collapse of the lung, the patient was given to inhale a mixture of 10% carbon dioxide in oxygen. This procedure induced hyperpnœa with moderate cyanosis. Skiagrams taken before the inhalation of carbon dioxide still showed the triangular shadow (fig. 2), but half an hour afterwards this was much less distinct, and two days later could not be appreciated (fig. 3). The physical signs (dense dullness, tubular breathing and whispered pectoriloquy) which, with one proviso, had remained unchanged until the administration of the carbon dioxide two and a half weeks after admission to hospital, were much less marked immediately afterwards and next day had entirely disappeared. The above referred to proviso was that at times tubular breathing was only slight and whispered pectoriloquy could not be heard: however, on getting the patient to cough and expectorate a very slight amount of mucus, these two signs immediately assumed their usually intense degree.

This case raises two points of interest. In the first place it shows how a similar appearance in the radiogram may arise from different pathological conditions. This triangular and mesially placed shadow can certainly be due to fibrosis of the lung, as in bronchiectasis, and to massive collapse of a portion of the lower lobe. A somewhat similar appearance may result from mediastinitis or mediastinal adenitis. Whether it can also be due to what is described as mediastinal pleurisy I am not sure. In this condition the fluid accumulates mesially instead of laterally. It has not been my lot to observe such a case. Savy and others [4] describe an encysted serous or purulent effusion in the mediastinal region of the pleura, but in these instances the hypotenuse is convex. This is of course what one would expect, at least if the fluid (serum or pus) were encysted and under pressure, although by analogy with the picture of simple pleurisy with effusion, in which the mesial edge of the fluid is shown by a concave line, it would seem possible that a non-encysted effusion in this region might be represented by such an appearance. From the point of view of diagnosis the important lesson for us is that the cause of a particular shadow in a radiogram of the chest cannot be decided without reference to the clinical history and the course of events.

The other point of interest in the case is the cause of massive collapse of the lung. This is a condition which has long been known to occur after bronchial obstruction, especially by a foreign body. In 1879 Lichtheim [5] said that it was common after croup and whooping-cough due to the blockage of the tubes with secretion and forcible expiration. In 1890 [6] Pasteur also drew attention to its occurrence after diphtheria. At first Pasteur ascribed the pulmonary collapse to paralysis of the diaphragm, but at a later date [7] he incriminated the elasticity of the lung and suggested the term "active pulmonary collapse." In 1914 [8] in his last paper on the subject, he defines this type of pulmonary collapse as "total deflation (as opposed to lobular or patchy collapse) of a large area of lung tissue, of sudden onset—in the absence of any signs of obstruction of the airway or of any known cause of obstruction due to failure of inspiratory power and attended by definite physical signs and symptoms." He appreciated that it might arise spontaneously, in association with inflammatory lesions of the lung and after surgical operations, and he said that it arose (1) in consequence of paralysis of the muscles of respiration (intercostals and diaphragm) when the collapse is usually bilateral, and (2) apart from paralysis, when it is usually unilateral.

Since that date, however, most writers have reverted to the older view that in some way bronchial obstruction is the cause. This was the opinion expressed by

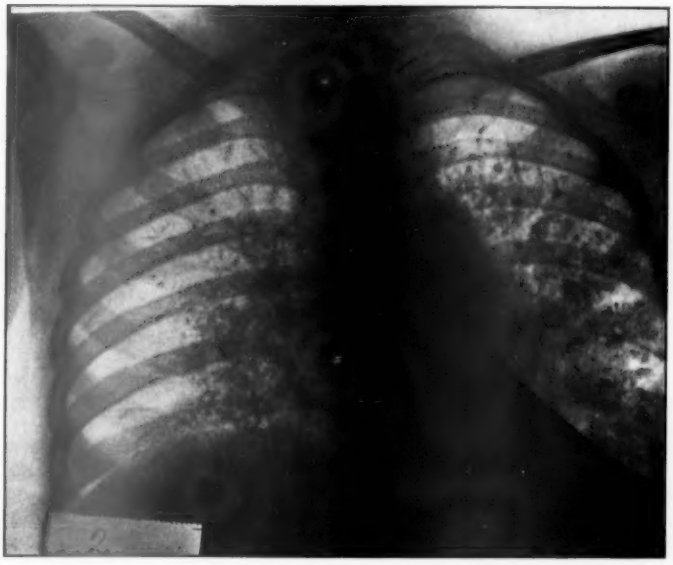


FIG. 2.—Skiagram taken just before inhalation of carbon dioxide, showing collapse still present.

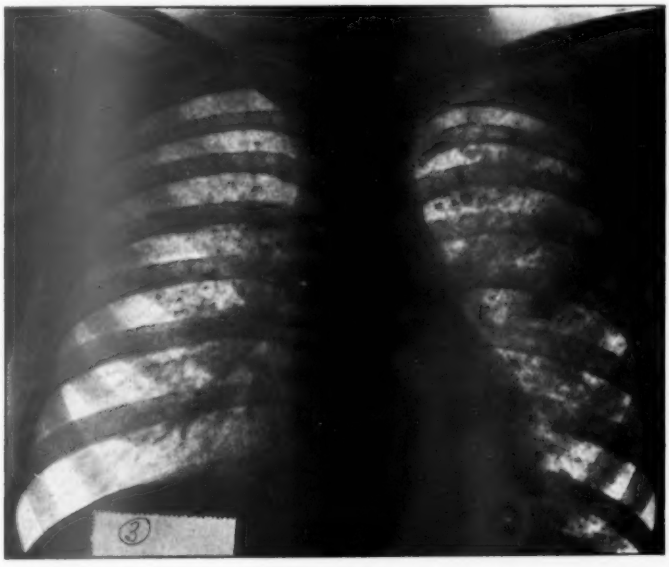


FIG. 3.—Skiagram taken two days after inhalation of carbon dioxide, showing that collapse has disappeared.

Elliott and Dingley [9] in 1914 in consequence of an investigation of a series of post-operative cases. According to these writers the obstruction was due to increased secretion and swelling of the mucosa.

The condition of pulmonary collapse was frequently observed during the Great War in gun-shot wounds of the chest, and Rose Bradford [10] believed that it was due to spasm of the bronchial muscles. Chevalier Jackson and Lee [11] have also lent their support to the theory of bronchial obstruction, and record cases in which bronchoscopy and removal of mucus gave relief. It may be here noted that recovery in the cases of Jackson and Lee was unduly slow and nothing like so rapid as described by Woodburn Morison and myself.

No one will deny that bronchial obstruction (e.g., by a foreign body) will bring about pulmonary collapse from absorption of air imprisoned behind the obstruction, or through the obstructing foreign body acting like a ball-valve, but that this is the way in which massive collapse usually arises cannot, I think, be entertained seriously. To my mind, apart from any other consideration, the rapidity with which the collapsed lung can be re-inflated (as was done in the case described above, and has been described frequently in the literature) by causing the patient to take sudden and deep breaths (this is the object of the administration of carbon dioxide) completely disposes of such a theory of ætiology. If the determining factor were a plug of mucus in the bronchial tree then deep inspirations would, by forcing the "plug" deeper into the bronchial tree, make matters worse rather than better.

In my opinion, the theory recently suggested by Woodburn Morison better than any other fits the conditions of onset, the course of the disease, and the effect of certain therapeutic measures. Woodburn Morison recalls the fact that the lung is in reality a muscular organ, and in his view the condition of massive collapse (he would prefer the term active collapse) of the lung "is a reflex disturbance of the sympathetic and vagus innervation of the lungs." Through over-action of the sympathetic, brought about by many causes, there results "dilatation of bronchi with cessation of the wave-like movement and a consequent accumulation of mucus. The balance between the sympathetic and vagus may be quickly restored and the condition rapidly clear up with return of cough and the expectoration of mucus. On the other hand, as the over-action of the sympathetic passes off, the vagus may reassert itself too strongly and cause a sudden spasm of the musculature, involving the whole lung, or a lobe of the lung or even, in rare cases, both lungs. It is not necessary to conceive of the spasm persisting any great length of time; it not only empties the lung tissue more or less of its air content, but when the walls of the alveoli and terminal bronchioles are brought into apposition the molecular adhesion effectively prevents the re-entry of air." With such a conception the suddenness of onset and the almost equal suddenness with which it disappears on deep inspiration are understandable. Woodburn Morison draws an analogy between the post-operative pulmonary collapse and the post-operative acute dilatation of the stomach.

[The skiagrams in this case were taken by Dr. Leggatt, radiologist to the East London Hospital for Children.]

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Intrathoracic Tuberculous Abscess as a Sequel to Pleurisy with Effusion.—Leonard Findlay, M.D.

The patient is a boy, aged 6 years 2 months, who enjoyed good health till the age of 4½ years, when he developed measles complicated by broncho-pneumonia. Three months later (November, 1929) he was taken ill suddenly with pain in the left

side of the chest and was admitted to the Evelina Hospital for Children on December 6, when a left-sided pleurisy with effusion was diagnosed. This was confirmed by X-ray examination and exploratory puncture, 30 c.c. of a straw-coloured fluid being withdrawn. No organisms were detected either in film or on culture of the fluid, but the cells composing the deposit were in great part (92%) lymphocytes.

While in the Evelina Hospital he developed scarlet fever and was removed to an isolation hospital on January 6, 1930. After recovering from scarlet fever he was transferred to the East Anglian Sanatorium, Colchester, where he remained for five months. On his return home he seemed perfectly well and attended school, but soon afterwards he commenced to lose weight and to suffer from night sweats, and for three weeks before coming under observation at the East London Hospital for Children, on May 20, 1931, he had been troubled with a cough.

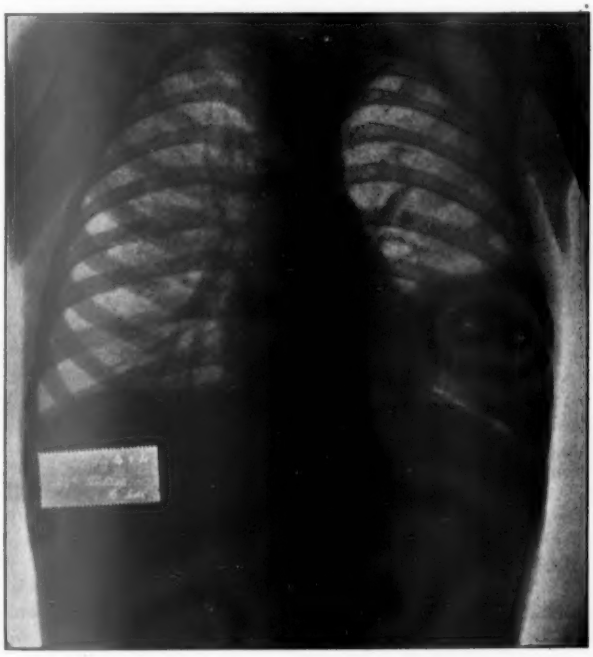

FIG. 1.—Intrathoracic tuberculous abscess following pleurisy, with effusion.

On admission to hospital he was noted to be a spare but well-coloured and well-developed boy. Temperature, pulse and respiration were normal. Examination of the chest revealed impairment of percussion note at the right apex in front, and dullness with deficient respiratory movement at the left base behind. Grocco negative.

Physical examination otherwise negative. Mantoux positive.

X-ray examination of the chest revealed a somewhat elliptical shadow of the size of a tangerine orange at the left base—this was slightly above the diaphragm and in contact with the chest wall suggesting an encysted collection of fluid—? empyema. There was no apparent disease of the ribs and the lung fields generally were normal.

The chest was explored posteriorly midway between the angle of the scapula and spine, with negative result, and again, just below the angle of the scapula, when

30 c.c. of a thick purulent material were removed: microscopically, this failed to reveal any cellular elements or organisms and no growth was obtained on culture. Three weeks later the chest was again explored, when 20 c.c. of the same thick purulent material were drawn off, and on this occasion a careful search discovered the presence of tubercle bacilli.

In the matter of terminology some might have preferred the title of empyema, or at least encysted empyema. There is little doubt that the lesion is probably situated in the pleura, but the term empyema suggests an accumulation of pus, and in this case, although the material removed by puncture had the naked-eye appearance of pus, it was devoid of all cells and pyogenic organisms: it was simply liquefied caseous material and identical with the contents of a cold abscess.

This sequel to pleurisy with effusion in childhood must, I think, be very rare, and it is on this account that I have brought it under the notice of the Section. Of 153 examples of pleurisy with effusion in childhood I have only known of one instance which had any similarities with this case. This affected a boy who came under my care at the age of 7 years, and who, after recovering and remaining apparently well for six months, was admitted to another hospital with what was diagnosed as tuberculous empyema. Unfortunately I have no details of the conditions found at this time.

Although one appreciates that pleurisy with effusion is of a tuberculous nature, and that the pleura is the seat of tubercles, it is in the lung that one anticipates a recrudescence. In the adult, according to Bowditch, Hedges and Cabot and Hammon [1] 30 to 40% of examples of pleurisy with effusion develop subsequently tuberculous lesions, most frequently in the lungs. Recrudescence of the mischief, however, either in the lungs or elsewhere, is rare during childhood. Dr. Stanley Graham [2] analysed in 1925 the after-histories of 56 cases of pleurisy with effusion admitted to my wards in the Royal Hospital for Sick Children, Glasgow, between 1914 and 1923. Of these 56 cases 39 were traced. It was learned that 3 patients had died, 2 from general tuberculosis one year after dismissal from hospital, and the other as the result of an accident. 32 of the children had remained perfectly well since their discharge from hospital, and on examination the only abnormality detected was a slight degree of flattening of the side of the chest which had been affected. In four children there had occurred at a later date another evidence of tuberculosis: two developed spinal caries one year later, one abdominal tuberculosis seven years later, and one (the case mentioned above) tuberculous empyema. This represents a development of subsequent tuberculosis in 15% of the cases, contrasting with the 30 to 40% quoted above in the adult. This benignity of pleurisy with effusion in the child is also shown in the results quoted from Pirquet's clinique by Nobel and Steinebach [3]. These authors found evidence of subsequent tuberculosis in at most 10%.

From a search of the literature I have failed to find any instance of such a sequel as I report. Most writers when discussing the sequelæ to pleurisy with effusion deal chiefly with the subsequent development of pulmonary tuberculosis. A striking exception, however, is Hedblom [4] writing from the Mayo Clinic. This author has written extensively on what he calls tuberculous empyema, and it would be interesting to hear how his views appeal to the Members of the Section, and especially to our President, who has a unique experience of the manifestations of tuberculosis.

In Hedblom's most comprehensive communication on this subject he reviews 71 examples. In 13 of these the condition followed on a serous effusion—in five within one year and in three cases within 2, 3 and 9 years of the onset of the serous effusion. On what grounds he diagnosed tuberculosis it is difficult to say—tubercle bacilli were never discovered in the sputum when obtainable, he makes no mention of the bacteriology or cytology of the "pus," and one of the cases was in reality a pyo-pneumothorax due to rupture of a tuberculous focus in the lung. But when this

author states that a serous pleurisy with effusion is apt to become purulent after it has been tapped several times, that any sterile empyema is probably tuberculous, and that empyema following artificial pneumothorax is most likely tuberculous, even although pyogenic organisms are present, I feel that his heterodoxy is ill founded.

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Dermatomyositis.—J. H. SHELDON, M.D., and WILFRID SHELDON, M.D.

The patient, a girl aged 9 years, is the third of four children. The other children and the parents are alive and well. There have been no miscarriages.

The patient was born at full term, and her development during infancy and early childhood was quite normal. A photograph taken at the age of 16 months shows a plump and healthy child. Measles occurred at 15 months and whooping-cough at 5 years. At the age of 7 years the child had an illness which was diagnosed as scarlet fever, but the mother states that the rash was like a nettle rash, and there was no peeling.

FIG. 1.

The child's health began to fail after this illness of "scarlet fever." Within a short time the ankles became painful and swollen, and the condition was called scarlatinal rheumatism. Stiffness of the joints then developed, and has been a constant symptom since that time. During the following year the child became moody and quiet and did not play with other children, although she continued at school until February, 1931, when she had influenza. She did not receive medical attention during this illness, but a few days later her hair began to fall out "in lumps." A pink discolouration round the eyes and of the hands and feet has been noticed since the scarlet fever.

Present condition.—The child is thin, weighing only 39 lb. The hair of the scalp has been almost completely lost, but is now beginning to grow again and is sparse and dry. Both eyes are surrounded by a halo of pink skin which is due to

a network of dilated capillaries extending forward slightly on to the cheeks. Dilated capillaries are also visible in the conjunctivæ (see fig. 1, p. 23).

Skin.—There is a diffuse bluish-brown mottled discolouration of the skin of the face, trunk and limbs. It is most obvious on the limbs, particularly on the legs, and at the hands and feet and rims of the ears gives place to a dull pink colour. When the extremities are allowed to hang down, the pink colour changes to a blue cyanotic tinge although the parts remain warm. Similarly if the child lies on her face the mottling of the face becomes more obvious. There is a dull brown erythema over

FIG. 2.

the back of the thighs and buttocks, spreading up to and parallel with both iliac crests (fig. 2). This rash fades on pressure but leaves some permanent brown staining of the skin. The skin over pressure points, such as the external malleoli, the distal ends of the fifth metatarsals, the elbows, and acromion processes (see fig. 2), is red, shiny and thin.

Over almost the entire body there is a loss of the normal skin elasticity. The skin feels as though bound down to the subcutaneous tissues, from which it cannot be wrinkled or picked up, and in this respect resembles scleroderma. The tightness of the skin is most obvious over the periphery of the limbs, and least marked over

the upper arms and on the back. The skin is particularly drawn in over the great trochanters.

Joints.—Limitation of movement of all joints of limbs. Shoulders and hips slightly less affected than elbows and knees. Knees have about two-thirds of their normal range of flexion; elbows cannot be straightened. Movement of the wrists and ankles is more impaired, the fingers have neither full flexion nor extension, and the toe movements are limited. Movements of neck and spine scarcely reduced. No creaking in joints. Skiagrams of long bones show general osteoporosis, but no deformity of outline.

Several septic teeth have recently been removed; those that remain are in good condition. Tonsils small, but tonsillar glands enlarged and firm. Heart, lungs, abdomen normal. Urine normal. Spleen not palpable. Epitrochlear glands palpable; other lymphatic glands not enlarged.

Nervous system seems to be normal. Tendon reflexes present. There is no pain or tenderness.

While under observation during the last three months the child has been afebrile.

Investigations.—Blood-count normal. A count on 14.8.31 showed R.B.C. 4,260,000; Hb. 85%; W.B.C. 12,000: Polys. 59%; lymphos. 41%.

Because of the light colour of the fæces, these were examined for evidence of pancreatic deficiency. Films showed "a fair amount of fat and undigested starch, a few undigested muscle fibres, no increase of pus or epithelial cells, no excess of fatty acids." The diastatic value in the urine was 10 units.

A small piece of skin was removed from the upper part of the left thigh. Microscopic examination shows a few circumscribed areas of small-celled infiltration in the corium, otherwise the section appears to be normal. Sweat glands are present.

Postscript.—Through the kindness of Dr. R. D. Lawrence, the following blood analyses have been carried out:—

Sugar, 83 mgm. per 100 c.c.; urea, 41 mgm. per 100 c.c.; calcium, 10·7 mgm. per 100 c.c.; phosphorus (inorganic), 4·4 mgm. per 100 c.c.; phosphatase, 0·189 units. These figures are within normal limits.

Allergic Enuresis.—GEORGE W. BRAY, M.B.

E. F., a girl aged 6½ years, was referred for investigation on account of—(1) persistent bed-wetting every night, with frequency and occasional lapses during the day, never having gained control of micturition; (2) papular urticaria since the age of eighteen months, and (3) pain in the epigastrium after meals, relieved by defæcation.

Past history.—Whooping-cough at 6 months, chicken-pox at 18 months and measles at 5 years.

Family history.—The mother suffers from migraine; as a child she had diurnal incontinence and has experienced rather precipitate micturition since. Her Wassermann reaction was positive until 1925, since when, as the result of treatment, it has been negative. The eldest daughter, aged 11 years, had a positive Wassermann reaction and was treated accordingly. She suffered from nocturnal enuresis until after the fifth year and still has occasional lapses. The second child is the patient. Before her birth the mother had further treatment and the Wassermann reaction has always been negative. The third child is a boy, aged 2 years, whose Wassermann reaction is also negative.

The patient had been treated with the usual dietary restrictions, the limitation of fluid intake, and being taken up at specified intervals to pass water. In spite of this the bed was always wet and improvement was lacking.

In previous cases investigated, the association of enuresis and papular urticaria

had been noted and the allergic basis of each verified. Skin reactions in this case showed a pronounced hypersensitiveness to the pork, ham, bacon and lard group of foods. The mother was instructed to remove these from the dietary as far as possible, and at the same time ephedrine was given in half-grain doses at bedtime. In two months the dose was reduced to a quarter of a grain, and at the end of the month will be discontinued.

As the result of this line of therapy there was a practically immediate disappearance of the spots, and during the first month the bed was only wet on six occasions, during the second month twice, on no occasion during the third month, only once during the fourth month during a very severe cold, and on no occasion during the fifth month.

I desire to convey my thanks to Dr. W. J. Pearson and Dr. D. N. Nabarro for referring the case to the Asthma Clinic at the Hospital for Sick Children, for investigation.

Persistent enuresis of allergic origin occurs generally along with such manifestations of hypersensitiveness as asthma, hay-fever, eczema and urticaria, and occasionally as the sole manifestation of allergy. This particular type of enuresis has many analogies with other manifestations of hypersensitiveness, for it tends to occur in bouts, to be worse at night, to be accentuated by fatigue and worry, probably due to sympathetic exhaustion, and to clear up on admission to hospital. In addition, the "shock" organs have a similar innervation, constrictor fibres being supplied by the parasympathetic system and inhibitory fibres by the sympathetic system. So stimuli that lead to bronchospasm may lead to the discharge of urine, and therapy that aims to stimulate the sympathetic to counteract the asthmatic tendency may lead to the cessation of a bed-wetting habit [1]. In some of my series of cases the sensitizing agent has been a food, in others such inhalants as feathers and horsehair, whilst in rare cases such a physical agent as heat or cold has been responsible [2]. The same allergen may cause both the enuresis and other allergy, or different allergens may be concerned. In cases without other manifestation of allergy if there is no urinary abnormality, and if emptying the bladder at specified times, dietary and fluid restrictions, and large doses of belladonna have proved of no avail, then the probability of an allergic origin should be considered, especially if there is a family history of allergy. In treatment we aim at the removal of specific allergens as determined by skin reactions or elimination diets, and the judicious dosage of ephedrine hydrochloride—to a child aged seven, half a grain for three months, a quarter of a grain for another three months, then cease.

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Infantilism with Local Overgrowth.—R. W. B. ELLIS, M.D. (for A. G. MAITLAND-JONES, M.D.).

W. N., female, aged 6½ years. The mother has had severe anæmia since the patient's birth. One normal sibling aged 8, alive and well. No family history of dwarfism. The patient was born at term weighing 1 lb. 6 oz. She then had a profuse growth of hair on her head, and this reached to the waist at the age of two years. Development as regards eruption of teeth, sitting up, and speaking was normal. She walked at two years. The first teeth decayed early and were extracted, the second teeth are appearing normally. The patient has been delicate and somewhat difficult to rear, but has had no serious illnesses and is usually happy and active, with a taste for dancing. She is of fair intelligence. She was shown by Dr. Maitland-Jones at a meeting of this Section in April, 1928, when she was three years old[1]; at this time she appeared relatively more prematurely aged, and a diagnosis of

[1] See *Proceedings*, 1928, xxi, 1326 (Sect. Dis. in Child. 74).

progeria was considered. She then weighed 9 lb. 12 oz.; height 26 in.; head 15 in.; the urine was normal and the blood urea 0·036%.

On examination.—An extremely small child of slender proportions, the large nose and teeth giving a somewhat parrot-like appearance. Height 33 in., weight 14 lb. 12½ oz. Skin rather dry but not wrinkled, hair thick and of fine texture. The nails are curved and their width is greater than their length. Extension of the middle and ring fingers of both hands is limited by contraction of the palmar fasciæ. The teeth are well formed and regularly placed. The anterior fontanelle is closed, the posterior fontanelle palpable.

Measurements: Circumference of head 15¾ in.; expanded chest (nipple level) 15⅞ in.; abdomen (umbilical level) 14¼ in.; length of upper extremity 14½ in.; length of hand, 4 in.; ant. superior iliac spine to internal malleolus 16 in.; length of foot 4½ in.

Blood-pressure could not be determined. Wassermann reaction negative.

W. N.: Showing relative undergrowth of mandible and overgrowth of maxilla and nose.

Urine: Reaction acid, albumin, slight haze; Fehling, no reduction; deposit—epithelial cells, amorphous urates.

Blood-urea (20.11.31): 0·058%. *Urinary urea:* (casual specimen) 2·4%.

Radiographer's report (Dr. Jupe).—Chest: No shadow in thymic area. Skull: The whole skull is very small; the fronto-parietal suture is not seen well but does not appear closed; occipital and sagittal sutures well seen. The sella turcica is normal in size relative to the skull. Hands and feet: No deformity of phalanges. Epiphyses not obviously delayed.

When this case first came under observation the diagnosis of progeria was considered on account of the prematurely old appearance, the early decay of the first teeth, and the precocious growth of long hair on the head. Subsequent development has not borne this out. The child does not show the characteristic bony deformities (e.g. disc-like terminal phalanges), hardening of arteries, or wrinkling of the skin. The thymus does not appear to be enlarged. There is

now a slight rise of blood-urea but this is unassociated with polyuria, and the urea-concentration is normal.

Mr. Hastings Gilford, in a personal communication, comments:

"This is not a case of progeria but of infantilism with local overgrowth and some progeric symptoms. The most prominent feature is the parrot-like physiognomy, due to relative undergrowth of the mandible and overgrowth of the maxilla and nose. This

W. N. with normal child of same age (6½ years).

type of physiognomy is essentially an exaggeration of the modern style. It is apparently determined by the atrophy of the organs of mastication—primarily and mainly the teeth—due to generations of inadequate use. This leads to unbalanced growth either of the whole front of the face, giving rise to the hatchet shape now so common, or, as in this case, to overgrowth of the upper face with enlargement and protrusion of the upper incisors, often associated with ill-development of other parts and sometimes of the brain, as in the Mad Hatter of 'Alice in Wonderland.' The overgrowth is of the same nature as that which occurs in rodents prevented from gnawing."

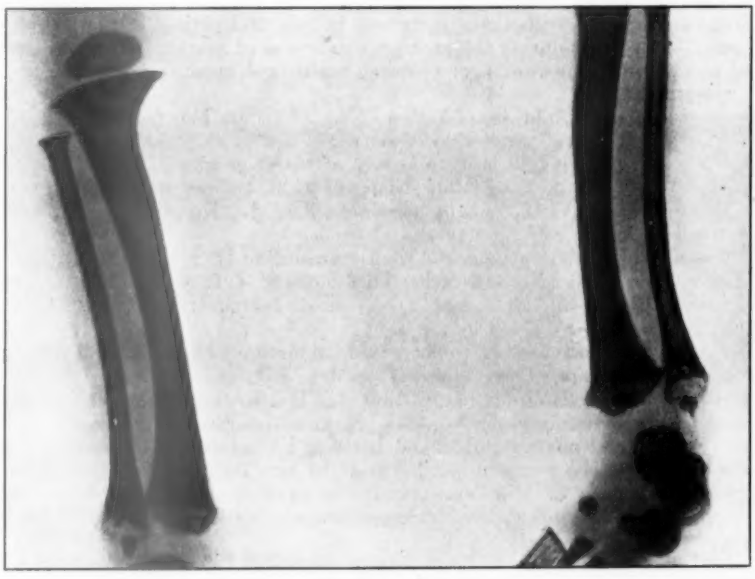
Renal Rickets.—REGINALD LIGHTWOOD, M.D. (by permission of HUGH THURSFIELD, M.D.).

A first child of apparently healthy parents was prematurely born, weighing only 3 lb. 8 oz. At the age of 1 year and 5 months he was brought to the Hospital for Sick Children on account of vomiting and failure to grow.

On examination.—Weight 10 lb. 10 oz. General appearance that of a small baby, well-nourished for its size and with a biscuit-coloured skin; contented and apparently in good health. Cardiovascular system, normal; blood-pressure, 60/90; respiratory system, normal; abdominal viscera, normal.

Skeletal system: anterior fontanelle wide open; no rib beading; double congenital talipes equinovarus.

Skiagrams (Dr. Shires).—Slight bowing of both legs with the following bone changes which are slight and not uniform in distribution: Irregularity and expansion of epiphyseal lines at lower ends of fibulæ, and similar but slighter changes at lower ends of femora. These appearances are suggestive of renal rickets (see fig.).



Renal rickets.

Investigations.—Urine: Clear, acid, albumin present, chlorides normal, no pus or casts, sterile.

Wassermann reaction, negative. Blood-urea, 77 mgm. per 100 c.c. Serum calcium, 12·3 mgm. per cent. (normal 9 to 11 mgm.). Blood phosphorus, 7·2 mgm. per cent. (normal 4 to 5·5 mgm.) Urea concentration test:

	Urea per cent.	Vol.	S.G.
Before urea... ...	0·625 ...	13 c.c. ...	1022
At 1 hour	0·55 ...	15 c.c. ...	1011

Course (during five weeks in hospital).—Temperature irregular (98·8° F. to 102° F.). There was vomiting from time to time. At first the weight rose to nearly 12 lb. and then it fell to 11 lb.

Summary. — Failure to grow; radiological appearances of renal rickets; albuminuria; nitrogen retention and high figures for blood calcium and blood phosphorus.

This case of renal rickets had been recognized at an unusually early age. In most

cases the condition occurs later in childhood, and especially from 6 years onwards, when growth in the long bones is taking place. If the possibility of renal rickets in infancy were recognized the condition would, perhaps, be discovered more often. Clinically the combination of failure in growth, a brownish yellow skin and albuminuria should suggest the possibility of this disease.

Mikulicz's Syndrome. — R. W. B. ELLIS, M.D. (by permission of A. G. MAITLAND-JONES, M.D.).

K. W., female, aged 7 years. Eleven siblings alive and well. One died from congenital morbus cordis; patient is a twin. Infancy was normal; measles at 18 months, scarlet fever at 6 years. Fourteen months ago gradual painless enlargement of both parotid glands occurred, unassociated with any constitutional disturbance. Swelling has persisted, with slight variations in size, and patient has been sent home from school four times during the past year as a case of mumps. Tonsillectomy has caused no change in the swelling. General health and appetite have been poor; no other symptoms.

On examination.—Child is of rather poor physique but not wasted. Weight 48 lb. There is bilateral swelling of the parotid glands with tilting forward of the lobe of the ear; the glands are uniformly soft and painless. Both submaxillary glands are palpable (the left smaller than the right); there is no alteration in size on swallowing water. Lachrymal glands not enlarged. No evidence of oral sepsis. Spleen not felt.

Wassermann reaction, negative. Mantoux reaction (1 in 1,000), negative.

Blood-count: R.B.C. 5,000,000; Hb. 66%; C.I. 0·66: W.B.C. 6,000. *Differential.*—Polys. 45·0%; eosins. 1·5%; small lymphos. 13·0%; large lymphos. 37·5%; large hyal. 3·0%.

In a second case at present under observation, the patient, a somewhat debilitated girl aged 9 years, shows bilateral painless enlargement of the submaxillary glands which has persisted for many months. Her mother has bilaterally enlarged lachrymal and submaxillary glands and a previous history of proptosis. Apart from this there have been no symptoms, and there is no indication of a primary cause. These three cases—the first non-familial and the two latter familial—illustrate the "idiopathic" variety of Mikulicz's syndrome in distinction from those cases in which there is a demonstrable primary cause—leukæmia, syphilis, sepsis, or otherwise.

Coarctation of the Aorta.—A. C. HAMPSON, M.D.

R. M., male, aged 12 years, was admitted to the Dreadnought Hospital for epistaxis. The bleeding had been profuse, and on the evening of admission he vomited $2\frac{1}{4}$ pints of clotted blood. At the age of 6 he had previously been in hospital on account of epistaxis and vomiting of blood, and during the year preceding admission nose-bleeding had occurred on three occasions. A diagnosis of valvular disease of the heart is said to have been made at birth.

On admission.—Hæmoglobin 40%; colour-index 0·8; white cells normal; blood-platelets 390,000 per c.mm.; bleeding-time normal.

Physical examination.—Apex beat $\frac{1}{2}$ in. to left of mid-clavicular line; area of cardiac dullness extended $\frac{1}{2}$ in. to the right of the sternum. At the level of the first space, dullness could be detected 1 in. to the right and to the left of the mid-line. A systolic murmur could be heard over the whole of the præcordium, being at a maximum in the fourth left space, about $\frac{3}{4}$ in. to the left of the sternum. The murmur was not associated with a thrill. At the base a soft diastolic murmur could be heard.

Pulsation in the carotid arteries was marked, and pulsation could be detected in the internal mammary arteries. The intercostal arteries were visible in the third and

fourth spaces, and an arterial anastomosis was very obvious round the angles of both scapulæ.

The blood-pressure in both arms was 145 systolic, and 75 diastolic, while that in the legs was 88 systolic; the diastolic could not be determined.

The spleen was not enlarged, and there was no evidence of purpura.

A diagnosis of coarctation of the aorta was made.

An Infant with Deformed Ears.—CECIL P. G. WAKELEY, F.R.C.S.

Margaret N., aged 3 months; family history not known; child believed to be illegitimate, and sent to the Belgrave Hospital for Children from a Home. Details of birth not known.

Deformity of right thumb.—The thumb was represented by a soft process, 1 in. in length and devoid of skeletal structures; the first metacarpal bone is also absent. The fleshy thumb-appendage could be easily twisted on the narrow pedicle, and it was removed when the child was 7 weeks old.

Small left ear showing accessory lobe in front of the tragus.

Right ear showing accessory lobes.

Deformities of auriculæ.—The auricula on the left side is much smaller than the other; the margin of the helix is inverted and curled inwards to hide three-fourths of the pinna. There is an accessory lobe of loose, soft tissue situated in front of the tragus and growing outwards from it.

The right auricula is large in comparison with the other, and the helix is broad in its superior margin, but nothing very suggestive of a Darwinian tubercle can be made out. There are two small accessory lobes above and below the tragus.

The left side of the face is flattened, and the lower jaw deformed on the left side, possibly due to a fracture of the horizontal ramus at birth.

The action of the muscles does not seem to be impaired.

Large Ovarian Cyst in a Girl aged 8 years.—CECIL P. G. WAKELEY, F.R.C.S.

Elsie B., aged 8 years, had been habitually constipated since the age of 5 years, but otherwise had enjoyed good health. On November 20, 1931, she was seized with abdominal pain, and vomited several times; this was followed by some loose motions. The pain only lasted a few hours, and the child played with other children, and appeared quite normal.

When her mother was bathing her she noticed a swelling in the abdomen; this had never been seen before. The child was sent up to hospital, where she was found to have a large, hard abdominal tumour about the size of a small coconut. It was movable from side to side, and slightly from above downwards, but it could not be moved further than the brim of the pelvis; it appeared to be cystic in places. Since the appearance of the tumour the child's bowels had acted normally each day. Rectal examination was negative.

The history is all-important in this case, because I consider that the cyst was within the pelvic cavity, and was the cause of the habitual constipation, until it suddenly rose out of the pelvis, and in so doing caused a certain amount of shock, which made the child vomit. The child's mother, who bathed her every night, would have noticed the swelling before if it had slowly developed in the abdomen.

POSTSCRIPT.—Operation was performed 2.12.31. The abdomen was opened through a right paramedian incision, and a large right ovarian cyst, weighing just over two pounds, was removed. The left ovary was normal.

Dr. Creed reported on the specimen as follows:—

"Histologically the tumour is a dermoid. There are a number of cysts present of varying sizes. One of the larger cysts is lined partly by columnar ciliated epithelium, and partly by a thick layer of stratified epithelium which, however, does not show much tendency to production of keratin; there is a sebaceous gland in relation to this stratified epithelium. There are a number of other cysts, some of which have lost their epithelial lining, and some, especially of the smaller ones, are lined by a columnar or cubical epithelium. Some of the cysts contain homogeneous pink-staining material, resembling thyroid colloid, but there is no definitely recognizable thyroid tissue present. There is some nervous tissue present, and there are areas of calcification."

Section of Radiology

President—Dr. J. M. Woodburn Morison.

[*November* 20, 1931.]

DISCUSSION ON THE X-RAY DIAGNOSIS OF DISEASES OF THE CHEST.

Dr. Stanley Melville: Recently in a medical journal I came across the following: "A heavy peribronchial infiltration of a beaded type in the upper part of the lung." This was a statement made by a clinician regarding the type of report he was in the habit of receiving. Why any of us write such arrant nonsense I know not, equally why anyone sends such comments to the press is difficult to imagine, but I suppose justifiable annoyance may account for it. All the same, such criticism may be just as well, lest we radiologists become too high-minded. It occurred to me therefore that I might open this discussion by a confession of the faith that is in me, and say what I have tried to learn by the combined study of pathology and radiology, and this with particular reference to two rather common heresies, namely, "hilum tuberculosis" and "peribronchial phthisis."

I regard all intrathoracic disease as a clinical study from beginning to end: this is possibly why I am so keen on team work. By this I do not belittle the value of radiography, for in this I believe we have the most definite, the most certain, and the most unmistakeable evidence of all the ancillary aids in diagnosis. Radiography is the eye of the clinician in internal medicine.

Pulmonary tuberculosis.—The position of radiography in the early diagnosis of this condition appears to me to be as follows: (1) Definite infiltration of the lung can quite readily be demonstrated on an X-ray film as soon as there is any definite clinical evidence. (2) When physical signs are present, it may be assumed that the initial stage has passed, and in these cases the X-ray film will usually reveal far more extensive involvement of the lung than is either suspected or can be revealed by the physical examination. (3) If we were dealing only with physical signs versus the X-ray film, the latter would be the safer guide. Fortunately for the patient, this is not the case, for the skilled chest clinician is armed with many more vital tests than merely percussion and auscultation. In pulmonary tuberculosis the vast majority of lung infection is by inhalation, and equally in the adult, the majority of investigators regard all further invasion of the lung as of the nature of a re-infection. I am aware that many deep thinkers regard tuberculosis much as they regard another of the infective granulomata, namely syphilis, in the sense that one stage of the disease invariably succeeds another, and that even after a long period of apparent inactivity, further manifestations may reveal themselves. In the school of thought to which most of us belong, I think there is much in favour of the theory of re-infection. The latter takes note of the acquired reaction peculiar to the previously infected person, the allergic state, so to speak.

Hilum tuberculosis.—In the infant, depending naturally upon dosage and resistance, the usual course is to get either an acute caseating broncho-pneumonia, so rapid and so fatal as to be hopeless from the first, or there may be a localized broncho-pneumonia in any part of the lung, but most commonly in the lower lobe, with which the name of Ghon has been closely associated. In the latter, the clinical evidence may be slight. The local area in the lung may entirely disappear or leave only a small oval or rounded calcified nodule. At the same time the tracheo-bronchial glands have reacted; they too, undergo calcareous change and the story is finished.

On the other hand, the glands may remain in a state of caseation and the second stage is reached in which the glands become the principal factor. Now, depending upon whether such caseating gland opens into a bronchus or into a blood-vessel or lymphatic, lies the future history. We get in the former, one or other of the two conditions mentioned above—truly a vicious cycle—or if into a blood-vessel or lymphatic, the typical miliary tuberculosis (fig. 1).

But there is a very interesting condition in association with the inflamed lymphatic glands, namely the stage of lymph-gland tuberculosis, which we must note. In this stage, in addition to the now definitely outlined glandular opacities, we may find a condition of involvement of the parenchyma, spreading outwards from the hilum. This is akin to the peri-focal inflammation which accompanies a tuberculous

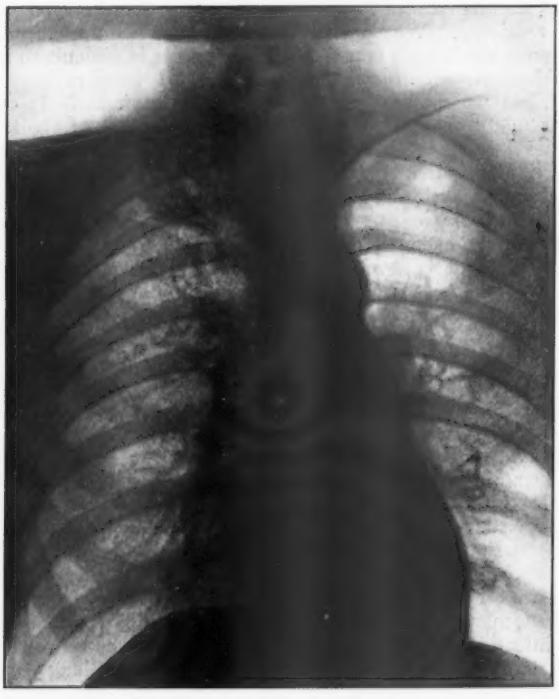


FIG. 1.—Miliary tuberculosis in an adult.

gland in the neck. This condition has been studied by many observers (clinicians and pathologists) and is known under many names: e.g., the collateral inflammation of Tendeloo; the smooth pneumonia of Virchow; the gelatinous infiltration of Laennec and the epi-tuberculous inflammation of many writers, among them Stoloff. Such appearances may be quite evanescent, disappearing within a few days, or they may be persistent or recurrent. Clinical symptoms may be slight or completely absent, but the infant reacts positively to tuberculin. This I would submit is an evidence of infection and not an evidence of an active lesion. To dub such an infant tuberculous, in the sense of having an active lesion, with all that such a radiological diagnosis entails, is, in my opinion, to be deplored (figs. 2 and 3).

Peribronchial phthisis.—This sad heresy is, I fear, the result of misguided

FIG. 3.—The same case showing complete disappearance some months later.

FIG. 2.—Epi-tuberculous inflammation showing the infected area spreading out from the hilum.

radiologists who in early days allowed themselves to be over-impressed by exaggerated shadows, to which they ascribed a pathological significance. On such a diagnosis, hundreds of Russian and Polish residents in the East End of London escaped military service during the Great War. The fact that linear striation in the lungs is composed not only of bronchi but of blood-vessels and lymphatics, seemed to have been overlooked. Again a simple chronic bronchitis may result in thickening and fibrosis of the bronchial walls with enlargement of the hilar glands and, if there has been any ulceration, we may find streaking of the sputum. Are we justified then in calling this condition by the alarming name of peribronchial phthisis? I trow not (fig. 4).

FIG. 4.—So-called peribronchial phthisis; a typical case of bronchitis and emphysema.

Abscess of lung.—The common causes of lung abscesses are: (1) aspiration, as from the inhalation of a foreign body; (2) embolic, e.g., following tonsillectomy; (3) following chronic pneumonia, though many of such cases are really the result of bursting into the lung of an interlobar empyema; (4) perforation from without, as in hepatic abscess; (5) breaking down of lung tissue in carcinoma or even in bronchiectasis.

The picture of a lung abscess is well known to us all. There is a fairly well-defined rounded opacity surrounded by normal lung tissue. Very soon the centre breaks down and shows a clearer area in the centre. If the abscess communicates with a bronchus, air will gain entry, and any fluid present will be shown to follow gravity.

In the case which I show you, the abscess complicated a basal carcinoma; indeed,

the abscess was the prominent feature in the case. There was marked toxæmia, and it was only by the aid of lipiodol that we were able to make a tentative diagnosis. The peculiar form of stenosis in carcinoma was, as you will see, present. At the subsequent autopsy, a large bronchial gland was discovered, which was definitely carcinomatous, and, on careful examination, the edge of an extremely friable lung was also found to be carcinoma (fig. 5).

Benign neoplasms of the lung.—It is only in the pathological sense that we can differentiate between benign and malignant new growths, for the benign neoplasm will in time deprive the patient of life by pressure. It is therefore of importance that we should appreciate this, and early diagnosis is of importance in view of surgical measures being advisable.

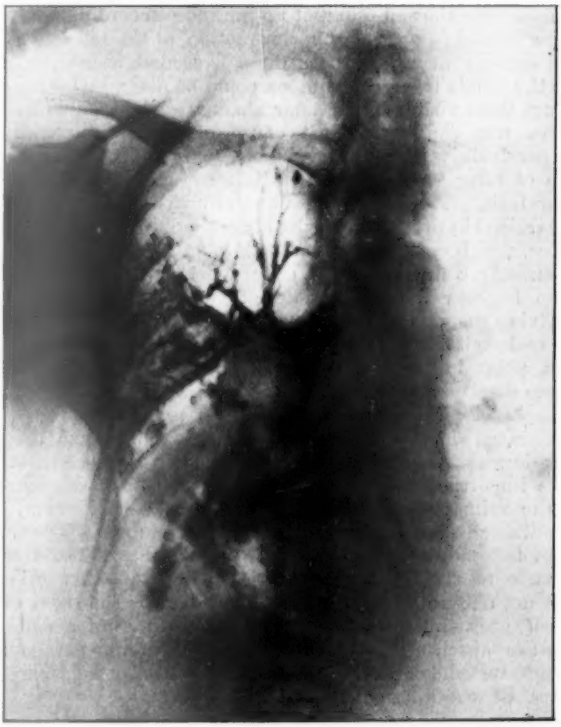


FIG. 5.—Stenosis of bronchus. The only definite evidence during life that a lung abscess was a breaking-down basal carcinoma.

All benign neoplasms are extra-pulmonary, but as they grow they push the lung, in front of them, and this is an aid in diagnosis.

The most common benign tumour is the fibroma, but lipomata and chondromata are met with, or sometimes a mixture.

Fibromata grow almost invariably from the posterior thoracic wall. They may grow to quite a large size without causing symptoms. The appearance is that of a well-defined rounded opacity, which is quite homogeneous in density, showing up in marked contrast to the surrounding tissues. The diagnosis is readily made by the simple expedient of collapsing the lung.

Teratomata and dermoid cysts.—Such tumours grow from the second or third branchial clefts or from the remains of the thymus, and are consequently always anterior in position. They are not so readily made out as are the fibromata, for they tend to irritate the surrounding lung tissue and are not always easy to separate at operation. They are usually irregular in shape and frequently contain bone, sebaceous material and hair, the coughing up of the latter being a definite clinical symptom. They are diagnosed by taking a film in the lateral plane, when it will be seen that the origin is from the mediastinum, and that they are growing anteriorly.

Dr. Peter Kerley said that the great difficulty was to find a classification. He adopted a simple radiological grouping: "root growths" and "lobe growths." The lobar or pneumonic form showed different appearances according to the lobe affected. The fissures were altered in position by contraction of the lobe. In the hilar form the opacity was densest near the root; often a second, less dense, opacity due to collapse covered the whole lobe. Carcinoma could be diagnosed with certainty if the vascular markings were visible in the hilar shadow and invisible in the peripheral area. Carcinoma was the commonest cause of bronchial stenosis in Europe. Diaphragmatic paralysis was a most valuable sign. The right phrenic nerve ran through a group of hilar glands while the left ran clear; hence the frequency of right phrenic paralysis. The paratracheal and bifurcation glands affected the vagus, disturbing the cardiac rhythm and causing abdominal symptoms, often gastric crises like those of tabes, which completely overshadowed the lung symptoms. Very rarely a lung cancer directly compressed the œsophagus and caused vomiting. Pleural effusion was the bugbear of the radiologist, for it masked nearly everything. Carcinoma involving the pleura caused such great thickening that it was impossible to tell it from underlying lung involvement.

The weakest point in the mediastinum was at the level of the third dorsal vertebra, and here displacements were seen. In fibrosis the œsophagus and trachea were always displaced and rotated. In collapse the trachea as a whole swayed slightly to the diseased side. Effusion soon depressed an atonic diaphragm, which pushed the liver down, often leading to a diagnosis of liver metastasis. The lung lymphatics were important to every radiologist. If the paratracheal group were easily visible the primary growth was probably extra-pulmonary. Tuberculous pneumonia, syphilis and aneurysm might simulate carcinoma, but were distinguished by the fibrosis of tuberculosis and by taking a film with a Potter-Bucky diaphragm and a harder tube to show aneurysm. Secondary infection of carcinoma was frequent but did not obscure the neoplasm. Occasionally the signs of abscess might obscure those of growth. A fluid level in the centre of a collapsed area was diagnostic. In the absence of enlarged glands or phrenic paralysis, diagnosis of malignant abscess rested on its asymmetrical position in relation to the area of consolidation and its connection to the mediastinum.

Hilum carcinoma showed as a dense opacity round the root, without collapse. It was easier to diagnose, but might rapidly be converted into the pneumonic form. Abscess formation was very frequent, but pleurisy was a late complication. Abscess did not obscure the diagnosis, as it remained the same size while the growth increased. A lobe might collapse and then this type could not be distinguished from the pneumonic type without a Potter-Bucky diaphragm. Obstruction of the vena cava was commoner in this type. Lymphadenoma and syphilis were the only conditions resembling it. Lymphadenomatous or lymphosarcomatous glands responded to a test dose of X-rays. Syphilis was always associated with gross interstitial emphysema. Secondary deposits might be confused with a form of pulmonary tuberculosis associated with diabetes; in this, however, a cavity might be seen and most of the nodes were in the upper part of the lung.

Dr. Maurice Davidson said that much of the difficulty sometimes experienced in the interpretation of radiograms of the chest, especially in non-malignant conditions, was due to the lack of unanimity in regard to a standard of normal control. He pointed out that in the training of students to recognize the evidences of disease, comparison with the normal was accepted in all branches of medicine as a basic principle. He realized that in chest radiograms taken from healthy persons the appearances varied within a wide range, but suggested that radiologists should set up in their lecture rooms a series of films taken from the chests of a number of individuals of different ages, occupations, sex, &c., who had never been in a doctor's hands and who were carrying on their daily work in the condition of body ordinarily described as good health. However much these skiagrams might differ, as they undoubtedly would do, from the ideal physiological specimen of a chest skiagram (which was perhaps rarely seen) they would nevertheless represent the various appearances compatible with the state which is ordinarily called health, and could, therefore, be taken as a useful standard of comparison in the study of the radiological aspects of disease. Health and disease, it must be remembered, were everyday terms with a practical connotation, and were, strictly speaking, arbitrary—rather than scientific—expressions.

[Dr. Davidson went on to refer to some of the difficulties in diagnosis associated with the presence of pulmonary abscess, and pointed out that this term was often used rather indiscriminately to cover a number of morbid conditions of which the ætiology and morbid anatomy were really distinct. He said that an abscess in the lung was often merely the expression of some other underlying disease, such as malignant neoplasm, and quoted a case of primary lung carcinoma of four years' duration in which the diagnosis had not been made during the life of the patient. He emphasized the point that there were many obscure chest conditions which could not be diagnosed either by X-rays alone or by clinical examination alone, and urged upon clinicians and radiologists alike the need for more constant co-operation in their work.

After showing various radiograms illustrating cases of intrathoracic malignant disease, Dr. Davidson exhibited some statistical tables which summarized the evidence for the view, which he himself held strongly, that the recent increase in the incidence of primary carcinoma of the bronchi and lungs was real and not merely apparent.]

Dr. R. E. Roberts said he agreed with Dr. Melville that radiology gave more certain, and often earlier, evidence of pulmonary tuberculosis than other methods of investigation, but he felt that in the early diagnosis of malignant disease it left much to be desired. It was disappointing to both surgeon and radiologist to find extensive pulmonary metastases developing within a few months of a radical operation for carcinoma mammæ immediately preceded by a negative radiological examination of the lungs. Radiograms were shown in which extensive primary or secondary intrathoracic malignant disease had developed within a few months of an entirely negative X-ray examination. Where the clinical evidence suggested intrathoracic neoplasm, a negative X-ray examination should be followed by bronchoscopy or possibly radiography after intratracheal lipiodol administration.

Another branch of pulmonary radiology which sometimes presented difficulties in diagnosis was the determination whether pneumokoniosis was complicated by tuberculosis or neoplasm.

[Skiagrams were demonstrated illustrating such cases, including one case in which silicosis was complicated by both neoplasm and tuberculosis.]

A further difficulty arose in the radiological differentiation between miliary tuberculosis of the lungs and acute miliary carcinomatosis.

[A case of the latter was demonstrated; the clinical evidence had been in favour of malignancy but this diagnosis was not definitely confirmed till a microscopic examination was made post-mortem.

In spite of the limitations of radiology in such cases as these, there was no doubt that this method of examination usually yielded a fund of information unobtainable by any other method, yet a close collaboration between clinician and radiologist was of paramount importance if mistakes were to be avoided.

Mr. J. B. Hunter: In the case of tuberculosis of the lung it is rarely the province of the surgeon to interpret the finer points of X-ray diagnosis, but he is chiefly interested in methods of collapse, and in one way he is assisted in cases in which the diaphragm is in spasm, in knowing that such a case is suitable for phrenicotomy. In a case of malignant disease one is often surprised on performing a thoracotomy for the insertion of radon seeds, to find the lung tissue greatly shrunken, bringing out the well-known point that there is a tremendous amount of collapse surrounding the tumour, and that often the X-ray appearances in no way assist in estimating the size of the tumour. In cases of abscess of the lung, where lipiodol injection has been carried out, the number of cases in which the lipiodol is found to run into the lung abscess is almost negligible. This is probably due to the fact that such an abscess, if opening into the bronchus, opens posteriorly or inferiorly, or there is some kind of valvular arrangement which prevents the oil gaining entrance. Where a dark shadow is present and a diagnosis of tumour—fibroma or cartilaginous tumour—is made, occurring in the upper lobe, it is often found that the shadow is thrown by a retrosternal goitre. If any such doubt should arise, a simple method of clearing up the diagnosis is to screen the patient while swallowing; retrosternal goitres will always move with the larynx, whereas the other tumours will remain stationary.

Dr. R. A. Young said he did not agree with the statement that X-rays might give the earliest indications of tuberculous disease in the chest. He was strongly of opinion that the earliest indications were obtained by clinical investigation, either from symptoms or by the finding of tubercle bacilli in the sputum. The earliest lesions in this disease in the lung were microscopic, but might be sufficiently definite to produce bacilli in the sputum at a very early stage.

Radiologists should be careful in putting down miliary tuberculosis as an explanation of some of the finer shadows that they saw in the lung, at any rate in the absence of confirmatory clinical findings. He had seen several cases in which great anxiety had been caused by an X-ray report of extensive miliary disease in one or more lobes, when the patient was quite afebrile, and the sequel proved that there was some other explanation of the shadows.

He wished that radiologists would produce a general, but not stereotyped, form of report.

X-rays were of great value in demonstrating interlobar conditions, particularly interlobar empyema and sometimes interlobar serous pleurisy. In his opinion a strictly lateral skiagram was of great value in localization; often almost more valuable than stereoscopic films.

He believed that malignant disease had been gradually on the increase in recent years. He could not accept the explanation that improved methods of diagnosis were responsible for this increase, which was apparent rather than real. In former days, though clinicians might have missed the malignant character of some cases experienced pathologists and morbid anatomists must have recognized them.

He maintained that teratomata were commoner than was generally supposed. One might hesitate sometimes to put the patient to the risk of an operation when they were found, but he was convinced that it was the right thing to do, both because the teratoma acted as a marked irritant to the lung tissue round it and to other structures, and also because it could become malignant. He had recently seen a case in which a teratoma, apparent in a skiagram taken ten years ago, had been allowed to remain, and when, owing to increasing changes in its neighbourhood, operation was carried out a few weeks ago, it was found to have become malignant.

Section of Laryngology.

[*December* 4, 1931.]

DISCUSSION ON THE TREATMENT OF MALIGNANT DISEASE OF THE HYPOPHARYNX.

Wilfred Trotter: TREATMENT BY EXCISION.—Cancer of the pharynx presents to the surgeon a problem as urgent as it is difficult. The disease is far from uncommon and its natural course is painful, repulsive and always fatal, so that it may well be regarded as one of the worst affections of middle age. For the surgeon the pharynx combines three of the most formidable obstacles to the the exercise of his art: it is inaccessible in a high degree, it is the seat of delicate and concentrated function, and it contains septic material to which the surrounding tissues are in no way immune.

In spite of these difficulties, it can fairly be said that during the last twenty years a certain degree of progress has been made in the attack on the problem, so that a number of persons have enjoyed some years of good health or are still living, all of whom, without treatment, would have died within a few months. Two lines of treatment have contributed to this modicum of success: first, surgical excision of the disease, and secondly, radiotherapy—usually combined with some form of surgical intervention. In this paper I shall deal solely with the method of plain excision with the knife. This will be because a single theme lends itself to easy exposition and because my experience of this method is by far the longer and the more extensive, and not at all because I have any doubt that radiotherapy is a valuable addition to our resources in treating cancer of the pharynx.

The term hypopharynx is not always used in the same sense. I have been accustomed to denote by it the tubular or post-cricoid part of the pharynx, a segment which, from the physiological and the clinical points of view, deserves a distinct name. For the purposes of this discussion, however, it may be more convenient to accept the extension of the word to all the pharynx that lies below the epiglottis—that is, to the so-called laryngeal part of the pharynx. The region thus denoted has, moreover, from the surgical point of view, a unitary character, in that access to the whole of it is to be got by a single operative method, the lateral transthyroid pharyngotomy.

With the exception of a few rarities, malignant disease of the hypopharynx thus defined is always a squamous epithelioma, and it will be assumed throughout this paper that this is in every case the lesion.

Clinical types of the disease.—Such progress as has been made in the attack on malignant disease of the pharynx has been contributed to by three chief factors, first a satisfactory method of access, secondly the control of post-operative infections, and thirdly a knowledge of the natural history of the disease itself. As has frequently happened in other departments of surgery, when it became possible to expose and explore the region with reasonable safety and precision, fresh light at once began to appear on the behaviour of local diseases. It soon became obvious that the disease occurs in well-defined clinical types the exact recognition of which is of great importance in prognosis and treatment. The types can be learnt more

effectively from experience gained in actual operative exploration of the pharynx than from the most careful clinical examination.

The value of recognizing these clinical types is so great that what I have to say will consist chiefly of a brief description of them. In order to be more concrete I shall describe at least one case of each.

Epithelioma of the hypopharynx has five common starting points, in the following order, from above down—the aryepiglottic fold, the pyriform sinus, the lateral wall, the posterior wall, the post-cricoid region. Although all these points are not far removed from one another, growths originating in them differ widely in symptoms, in prognosis, and in the details of treatment.

Growths of the aryepiglottic fold.—These constitute one of the classical and generally recognized types of so-called extrinsic laryngeal cancer. It is favourable in that it causes early hoarseness and stridor, and lends itself in early cases to removal without serious mutilation. I may mention in illustration a hospital patient referred to me by Sir StClair Thomson.

Case I.—Stout plethoric man, over 60, with chronic bronchitis. Typical epithelioma of aryepiglottic fold, mass of glands in the neck on the same side, so large that it had been regarded as a lipoma. Two-stage operation, glands first then later lateral pharyngotomy and excision of primary growth. Patient recovered with no residue of the operation except some hoarseness. Seven years later he developed an epithelioma on the *opposite side* of the pharynx; the scar of the operation in the mucous membrane was still visible and quite healthy.

Growths of the pyriform sinus.—These are extremely common and are of evil repute, not so much because they are inherently difficult to cure, as because the diagnosis is not usually made at an early period. The growth, on account of its station in a recess of the pharynx, causes at first but a slight though persistent sense of discomfort, and may escape discovery with the laryngoscope. It is not uncommon for the patient to be seen first when there is already a mass of hopelessly fixed glands. With the extension of the growth into the lumen of the pharynx, symptoms become severe.

I may perhaps mention here a case in which the growth was in this situation, not, however, as typical of its class, but because of the exceptional interest of the origin of the growth. The patient was referred to me by the late Sir Felix Semon.

Case II.—The patient had been operated on some six years earlier for an epithelioma in the floor of the mouth. He now had a rounded swelling by the side of the upper opening of the larynx and occupying the pyriform sinus. It showed a superficial ulceration. The swelling was removed by local excision. It was pronounced by the late Professor Shattock to be a squamous epithelioma, possibly growing in a lymph node and therefore perhaps a recurrence from the mouth. The patient recovered with normal function and survives without recurrence after over 20 years.[1]

Growths of the lateral wall.—These constitute undoubtedly the most important type that has been revealed by operative exploration of the pharynx. Its importance resides in this—that while it is extremely amenable to treatment by excision, its exact nature is often overlooked and an unfavourable view taken of the prospects of treatment. The growth begins in the lateral wall at about the level of the apex of the arytenoid but well away from the upper laryngeal opening. As it develops, its anterior edge sooner or later involves the arytenoid and lateral wall of the larynx. In its earliest stages it can be removed without interference with the larynx, and the pharyngeal wall can be sutured completely. The growth projects inwards and overhangs the arytenoid, the vocal cord and the upper laryngeal opening on the same side, thus often leading to a mistaken diagnosis of a primary aryepiglottic or

[1] In this case the operation of lateral transthyroid pharyngotomy was used for the first time.

pyriform sinus lesion. When it is of fungating type the appearances are far more formidable than the actual state of affairs. Since there is no primary involvement of the arytenoid, the vocal cord remains movable to a late period and this late mobility of the cord becomes of the utmost prognostic importance. Whenever therefore the cord remains movable, operation should always be considered, however grave the general picture may be. A special difficulty in diagnosis comes from the fact that the cord and arytenoid are often completely hidden by the projection of the tumour.

The importance of this type seems to me so great that I may perhaps be allowed to quote several cases illustrative of it.

Case III.—A hospital patient admitted on account of severe stridor and difficulty in swallowing; laryngoscopic examination showed the pharynx at the level of the upper opening of the larynx to be filled by a yellow sloughy mass which concealed the vocal cords but seemed to be attached laterally. The tumour was removed by lateral pharyngotomy. It involved the arytenoid region and was thought at the time to have arisen in the ary-epiglottic fold; further experience, however, makes it practically certain that this was a true lateral wall growth. The patient recovered with good function; he failed to report after five years, but at that time there was no recurrence.

Case IV.—A man of 57 referred to me by Sir James Dundas Grant. Typical lateral wall growth projecting moderately inwards but with movable cord. An unfavourable subject with

Epithelioma of right lateral wall (moderately early) removed by local excision. No disability and no recurrence after seven years. (*Case IV.*)

chronic bronchitis. Local excision by transthyroid pharyngotomy. The patient recovered with normal function and has no recurrence after seven years. (See fig.)

Case V.—A man aged 62 referred to me by Dr. George Cathcart. The patient was somewhat plethoric in type, with a tendency to chronic bronchitis. A typical right-sided lateral wall growth of large size was present. A very large mass of glands extended from the mastoid to the clavicle. This was on the whole the most formidable looking case of pharyngeal malignant disease I have ever operated on. The glands and primary growth were dealt with at one operation. The primary growth had come through the wall of the pharynx and was fixed to the ala of the thyroid which was therefore removed in continuity with it. The patient recovered with normal function, apart from a partial fixation of the right cord. Six years after the operation he developed an epithelioma of the gum on the upper jaw where a dental plate had caused ulceration. This responded to radiotherapy at the hands of Dr. Finzi. There has never been any sign of recurrence in the pharynx or glands up to the present time—one month short of seven years since the operation.

Case VI.—A man, aged 56, with a really early lateral wall growth well away from the arytenoid region. Treated by local excision with immediate closure of the pharynx.

Recovery with normal function. The patient remains free from recurrence three and a half years after operation. The case is mentioned after the comparatively insignificant period of three and a half years only to illustrate my confidence that with this type of growth treated in this way one may regard a cure as practically certain.

Growths of the posterior wall.—The three types we have already considered are practically confined to men. With the posterior wall we come to a region where the liability of women to carcinoma of the pharynx begins to appear, though in this type men still predominate. The growth is seated on the posterior wall with but little inclination to one side; its upper limit may be at or a little above the level of the tip of the epiglottis, its lower limit may extend into the post-cricoid region. Although it is sometimes visible by direct inspection through the mouth, the disease is often overlooked in the early stages. The technical interest of this type lies in the fact that any excision of the posterior pharyngeal wall calls for an immediate plastic reconstitution by a skin flap.

Case VII.—A middle-aged female hospital patient. There was a large epithelioma on the posterior wall opposite the upper opening of the larynx. Palpable glands, later proved not to be epitheliomatous; unilateral gland dissection, followed at once by lateral pharyngotomy. A large area of the posterior pharyngeal wall was excised with the growth and immediately replaced by a pedicled skin flap. A secondary operation a few weeks later divided the pedicle of the skin flap and closed the pharynx. The patient recovered with normal speech and swallowing. Eight years later rapid and extensive local recurrence took place.

Growths of the post-cricoid region.—This type has three very remarkable peculiarities: it is a disease of women, it occurs in them at an age a good deal younger than does cancer of the pharynx in men, and it is often preceded by difficulty in swallowing, of slight degree but of many years' duration. It is a disease of symptoms, and its leading symptom is a rapidly increasing dysphagia which may be well marked when any examination, short of direct endoscopy, yields no evidence. Post-cricoid carcinoma contrasts strikingly with the disease in the next common seat below it—carcinoma of the cervical œsophagus. This is a disease of men and a disease of physical signs rather than symptoms, for it causes no early dysphagia and usually shows itself first by causing paralysis of a vocal cord and enlargement of the thyroid gland.

The post-cricoid carcinoma seems to vary in malignancy a great deal and its appearance is sometimes misleading, as is shown in the following illustrative case.

Case VIII.—Hospital patient, middle-aged woman of excellent physical and mental character. Typical post-cricoid carcinoma; diagnosis easily made by ordinary laryngoscopy. Lateral transthyroid pharyngotomy. The growth was extensive and almost encircled the pharynx. An unfavourable opinion was formed but the operation was carried out, a complete annular resection of the tube being done and extending from the arytenoids well into the cervical œsophagus. Immediate reconstruction by a pedicled skin flap, with separation of flap and closure of pharynx some weeks later. Patient recovered with good function. Apart from some occasional trouble from a fibrous stricture where the reconstructed pharynx joins the œsophagus, the patient remains well and free from recurrence nine years after the operation.

Operability.—The operation of local excision for cancer of the pharynx can be recommended with reasonable confidence only when the patient is edentulous, the growth is still confined within the pharyngeal wall, and gland involvement is limited, the glands being hard, well-defined and not fixed. It must be confessed that I have often defied these restrictions with impunity, and even in the illustrative cases I have mentioned there will be found two examples of extensive gland involvement and one example of extension through the pharynx to the thyroid cartilage. This

impunity, however, merely tends to show that within the requirements I have laid down the margin of safety is good. A greater severity must be insisted on with the post-cricoid carcinoma. There any gland involvement is very grave, and the other restrictions are indispensable to reasonable safety and a fair prospect of success. My experience suggests that, apart from post-cricoid cases, the seriousness of lymphatic gland involvement has been exaggerated.

Late recurrences.—Every advance in the surgical treatment of malignant disease has revealed a liability to recurrence at periods far later than had been suspected as possible from experience with more imperfect methods. This possibility is strongly shown even in the few cases I have quoted to illustrate my theme. I have mentioned a case of direct local recurrence after eight years, a case of an epithelioma near—but not at the site of—the original growth, after seven years, a case of an epithelioma appearing in the mouth six years after excision of one from the pharynx, and a case of an epithelioma in the pharynx six years after the excision of one in the mouth. In such a small group these four cases form a remarkable little series, in that the narrow limitation of the time of reappearance of the disease to the period between six and eight years after the primary operation applies both to true local recurrence and to apparently fresh outbreaks of the disease. The hypothesis that seems most satisfactorily to account for these facts is as follows. The growth of a cancer arouses resistance in the body of the patient. This immunity is not strong enough, except in rare cases, to check the progress of the disease, but when the cancer is, as we say successfully, removed, the relative immunity survives and can keep in check the minute doses of tumour left behind or the tendency for fresh cancers (of the same type) to start. In time, however, this immunity declines and in the case of the pharyngeal epithelioma reaches so low a grade in about seven years that surviving relics of the original tumour can assert themselves or a fresh outbreak occur.

However we may regard such a hypothesis, it is plain that estimates of the results of treatment based on periods of much less than seven years' freedom from recurrence can have only a limited value. This criticism must not of course be pressed too far, since periods of freedom far shorter than seven years and in no sense deserving to be called cures may, from the patient's point of view, be well worth having.

Results.—The final results of operative treatment must be considered from two points of view: (1) freedom from recurrence and (2) the condition in which the patient survives. Throughout the foregoing remarks I have tried to lay all possible emphasis on the value of precise local knowledge of the epitheliomas of the pharynx in dealing with them by operation. Such knowledge makes possible the exact orientation of any necessary operation and so increases the prospect of cure and at the same time diminishes the need for mutilation. The view is sometimes expressed that the more extensive an excision, the most likely is it to be successful; this is by no means necessarily true, for if the operation is not exactly oriented in regard to the growth, its mere extent is unlikely to save it from failure. This criticism applies to many cases in which extirpation of the larynx is practised in dealing with pharyngeal growths. There are, in my opinion, very few cases in which that formidable mutilation is of use in the treatment of such growths. Most of the cases in which the tumour cannot be got away without laryngectomy are incurable by any operation, and when the tumour can be got away by local excision the mere addition of laryngectomy gives no further security. It will be noticed that in the small number of illustrative cases I have mentioned the only residual disabilities left have been the occasional fixation of one vocal cord, and in one case some fibrous constriction of the œsophagus. I should not feel able to record as a true success the cure of a pharyngeal carcinoma won at the expense of laryngectomy. One of the most beneficent effects of the introduction of radiotherapy has been its tendency to make

us look with increasingly critical eyes at treatment by crudely mutilating operations.

With regard to the small number of actual results I have quoted, it must be understood that they are intended to be illustrative of the various clinical types of disease rather than to embody a full statement of experience. Such a statement to be satisfactory would have to be much more detailed and extensive. It would include some more successful results, a good many partial successes with freedom from recurrence up to about three years, and a considerable number in which the operation was fatal or a failure. The cases I have actually quoted may be put together in a list with a statement of the length of freedom from recurrence that followed in each case on the simple excision of the growth. In this way a more general view is obtained.

Case 1	...	Aryepiglottic fold (extensive glands)	...	Free from recurrence	7 years
Case 2	...	Pyriform sinus	...	,, ,,	20 ,,
Case 3	...	Lateral wall (large primary growth)	...	,, ,,	5 ,,
Case 4	...	Lateral wall (moderately early) ...	...	,, ,,	7 ,,
Case 5	...	Lateral wall (large primary ; extensive glands)		,, ,,	7 ,,
Case 6	...	Lateral wall (early)	...	,, ,,	3½ ,,
Case 7	...	Posterior wall	...	,, ,,	8 ,,
Case 8	...	Post-cricoid (extensive)	...	,, ,,	9 ,,

The eight cases thus show an average freedom from recurrence of over eight years. Even a group so small as this, especially when it is remembered that none of the patients suffered any serious mutilation, suggests that in suitable circumstances the method of plain local excision with the knife has a definite usefulness.

Professor von Eicken (Berlin) : Malignant tumours of the hypopharynx may be divided into two groups. The first group includes tumours arising from the lateral walls of the larynx, the outer surface of the epiglottis, the pharyngo-epiglottic fold and the plica aryepiglottica. The tumours of the second group take origin from the sinus pyriformis and the lowest parts of the hypopharynx.

The tumours of the first group develop more slowly and form metastases later than do those of the second group, which are of rapid growth and show early metastases in the regional lymph glands.

Recently the French school has proposed a division of these tumours into two groups which can be distinguished by their microscopical appearances. The first is the epidermoid or cutaneous type which is characterized by the presence of typical epithelial pearls and prickle cells. The second is the anepidermoid or mucous type, and it shows the so-called "Hollundermarkzellen," which are large polyhedral cells with so transparent a protoplasm as to produce a vacuolated appearance. True epithelial pearls are not present, but the laminated arrangement of the so-called "onion bodies," which are a constant feature of this type of tumour, may cause confusion ; however, a distinction is readily made when it is observed that well-marked nuclei are present. Both these types are found relatively often in the hypopharynx, but the mucous type is the more frequent.

Quick and Cutler have described a tumour which they term a transitional cell carcinoma. This tumour is similar in appearance to a lympho-epithelial carcinoma, but no lymphatic tissue is present. It shows round and polyhedral cells with very large bladder-shaped nuclei which have hyperchromatic nucleoli. These tumours develop very quickly, metastasize early in the glands and are very sensitive to ray therapy. They need not be discussed further here, as they do not occur in the hypopharynx, but are mentioned as an illustration of the general law that sensitivity to ray therapy stands in inverse ratio to the degree of differentiation of the tumour cells. The lympho-epithelial carcinoma provides the most frequent example of this law.

Tumours arising from the lateral wall of the larynx or from the sinus pyriformis may be readily diagnosed by laryngoscopy. It is often more difficult to recognize a

carcinoma of the post-cricoid region or of the lower hypopharynx. In early cases of this sort the laryngoscopic picture is normal, or at the most some swelling of the aryepiglottic fold may be discerned. It is in such cases that my method of indirect hypopharyngoscopy is of special value. The method of universal autoscopy devised by Seiffert also renders possible a complete inspection of the hypopharynx. In cases in which dysphagia is a symptom, the radiographic appearances, on the swallowing of some opaque medium, are of value. The areas of varying density in the medium as it passes the growth enable the extent of the tumour to be recognized. If the tumour fails to obstruct the food passage, Skalitzer recommends that the medium should be given with the patient in the prone position, so that it may pass the critical area more slowly.

Careful palpation of the neck in order to distinguish involvement of the lymph glands is of the utmost importance. Despite the most thorough examination, small enlarged glands which could not be recognized by clinical examination are often exposed at operation, lying along the jugular vein. At the same time, involvement of the glands which lie between the bifurcation of the carotid and the junction between the facial and internal jugular veins may be the first and only sign of hypopharyngeal cancer. This has been observed in 25% of my cases.

The prognosis in surgical intervention for carcinoma of the hypopharynx is unfavourable. Tumours which are limited to the lateral wall of the larynx have a relatively favourable outlook, as in some cases a total extirpation of the larynx may lead to lasting cure. Conditions are much less favourable in the case of a carcinoma of the sinus pyriformis and the deeper part of the hypopharynx. Gluck and Soerensen, those celebrated exponents of the art of laryngeal surgery, have indeed made extensive efforts to extirpate the disease by surgical measures. They have excised the larynx, a large segment of the pharynx and the corresponding lymphatic glands. This is a heroic intervention which patients are reluctant to undergo, for not only is the operation itself severe, but they must later submit to a series of plastic operations to remedy the resultant mutilation. Despite this objection many surgeons adopt the view that the otherwise hopeless outlook justifies surgical intervention.

Soerensen has reported on 125 cases in which he carried out laryngectomy and partial pharyngectomy. Of these, nine were permanently cured, that is, rather less than 10%. On account of the poor outlook this radical intervention has not been generally adopted. Soerensen himself condemns the measure if bilateral involvement of the glands is present. I shall not describe the various complications, such as extensive cellulitis, aspiration pneumonia and secondary hæmorrhage, as they are unfortunately only too well known to every surgeon who has carried out a series of these operations.

It is natural that, in view of the patient's immediate suffering and hopeless future, efforts should have been made to alleviate his lot by ray therapy. In other regions this mode of therapy has met with success, and I was encouraged to adopt this method by the astounding results I had obtained in cases of cancer of the vocal cords. In these cases direct application of radium-carriers to the tumour was made after access had been obtained by a window resection of the thyroid cartilage. In this work my clinic was assisted by the advice of Professor Halberstädter and by the zeal of my former chief assistant, Dr. Seiffert—now Professor in Kiel University.

The application of radium to tumours of the hypopharynx can be carried out in various ways.

(1) *External application with a pack.*—Either a pack or a modelled radium carrier may be employed at a distance of at least 3 cm. from the skin. The appliance remains in position for a week on each side of the neck. We have only

used this method occasionally, and then only as a preliminary to surgical intervention.

We have had remarkable success with this method in a case of extensive carcinoma affecting both true and false vocal cords; the patient has remained well for fifteen months.

(2) *Application of radium by the oral route.*—The radium-carriers are introduced on a long wire and placed in direct contact with the tumour. The method is technically difficult and does not permit a full dose to be exhibited; for this reason we have not employed it.

(3) *Radium combined with surgery.*—The area of the tumour and the posterior wall of the pharynx are exposed from the neck by an incision along the border of the sterno-mastoid muscle. When necessary, the omohyoid is cut through, as are also, after ligature, the common facial vein and the external carotid artery. Care is taken to avoid opening the pharynx. Three or four radium-carriers, each containing 10 mg. of radium, are distributed in the region of the tumour and the great vessels are protected by the interposition of sheets of soft rubber. The wound is completely closed. The radium-carriers are left in position for three or four days, that is, until a milligram-hour dose of 3,000 or 4,000 has been attained. The wound is then opened and, after removal of the radium and the rubber sheets, is again completely closed.

The radium-carriers are provided with a metallic filter for the γ-rays, and in addition have a 2 mm. thick rubber coating which serves as a secondary filter.

This method has been employed in eleven cases and in none has any complication been remarked although they have been observed for a long time.

In some cases this mode of therapy has been combined with the "Spick" method, in which thorium contained in fine gold capillary tubes is inserted into the tumour. Fine silk threads enable the tubes to be withdrawn at a later date, but as the emanations from thorium are only temporary, the tubes may be left permanently in position without ill-effects.

Of the eleven cases treated, two are free from symptoms and the tumour has completely disappeared. In five others the tumour has markedly decreased in size, but symptoms are still present. In the four remaining cases of advanced carcinoma with glandular deposits no success has been attained.

Radiotherapy.—The method of application of the so-called "tolerance dose" in one or a very few sittings has not had satisfactory results. The application of very large doses exceeding the tolerance dose leads to severe complications and fails to cure the growth. For the last ten years Coutard, of Paris, has employed a method which has been termed the "protrahiert-fraktionierte" method. He finds it possible to give a large dose in a comparatively short time. Treatment occupies three weeks and the patient is exposed to the rays for one hour daily.

I have had no experience of this method of treatment for cases of hypopharyngeal carcinoma. According to statistics which are as yet unpublished, Coutard has obtained permanent cure in 20% of his cases; much better results than surgical intervention can claim. Zuppinger has suggested that Coutard has made a careful selection of favourable cases from the vast material available in Paris, while the less favourable cases were dealt with in other clinics. If this criticism be justified it naturally rather detracts from the value of Coutard's results.

In 1930 Zuppinger together with Kahlstorff reported on their experiences with the "protrahiert-fraktionierte" method. The work was carried out in the Roentgen Institute of Professor Schinz in the Canton hospital of Zürich.

I quote from their paper as follows:—

"Our material does not permit us to give a final judgment on the value of this method. The cases have been observed for too short a time to permit of more than observation of the

immediate effect of the rays. Despite the very desperate cases in our series, we have obtained good palliative results and sometimes freedom from symptoms has been attained. These results are better than we ever obtained in our previous experience."

The authors had treated fourteen cases of carcinoma of the hypopharynx. Two of these cases had been rendered free from symptoms. The first was a case of carcinoma of the sinus pyriformis without involvement of the lymph glands; microscopical examination of the growth showed it to be a pavement-cell carcinoma. The patient was free from symptoms for nine months. The other successful case which had remained free from symptoms for eleven months was one of carcinoma of the aryepiglottic fold, also without involvement of the glands, and of similar histological structure. In nine other cases freedom from pain and dysphagia was attained. The authors are of opinion that these results alone justify the carrying out of the method and I refer those who are especially interested to the original paper and also to a monograph by Zuppinger which has lately been published.

In a personal communication, Professor Hegener, who has worked in Hamburg with the radiologist Holthusen, informs me that their results with the Coutard method in cases of carcinoma of the hypopharynx have been very promising.

Although the claims of Coutard have not yet been fully substantiated, it would appear that his work, and also the method of applying radium after surgical exposure employed in my own clinic, open up a more hopeful outlook for the therapy of carcinoma of the hypopharynx.

J. B. Hunter: SIGNS AND SYMPTOMS.—The symptoms of carcinoma of the hypopharynx are vague. Slight difficulty in swallowing is first noted. Painful swallowing may occur only in the late stage of the disease. In female patients, the difficulty, which has been present over a long period, is increased, and it is because of this prolonged difficulty that these patients are usually thin. Examination of the patient is difficult; frequently no growth is obvious on direct examination with the laryngoscope, and no patient with difficulty in swallowing over a few months should be dismissed without a direct examination. There are, however, certain small points that may give a correct interpretation by the indirect method. A pool of mucus, which is not cleared by swallowing, may be seen behind the larynx, or the edge of an ulcer, unseen in quiet breathing, can be made out on strong phonation. In other cases there may be œdema of the arytenoids, and usually both are equally swollen. This œdema is not to be taken as a sign of inoperability, as it does not indicate involvement with growth, but is merely a sign of a lesion in the neighbourhood, in the same way as the lower eyelid becomes œdematous. A digital examination should always be made, and valuable information can be obtained in this way, especially in cases of growth on the posterior wall. External examination of the neck will often afford valuable guidance to involvement of glands and thickening round the cricoid. The latter may determine the surgical procedure to be adopted.

Direct examination is necessary in cases of doubt, and in such cases no attempt should be made to pass the instrument beyond the ulcer. In my experience the results obtained by a barium swallow have been unsatisfactory.

Pathological types.—The type of growth is always a squamous-celled carcinoma and the primary growth is relatively benign, requiring but a small margin for its adequate removal, a favourable feature surgically. The degree of ulceration present appears to depend on the amount of sepsis to which the growth has been exposed, and there is frequently an apparently large area of submucous infiltration in the edentulous patient, whereas in patients with teeth, the whole area involved by the growth is ulcerated. Glandular involvement is, on the whole, early, but not intense. Where the glands are fixed and inoperable the primary growth has reached an advanced stage. In this, growths of the hypopharynx differ from other carcinomas of this region.

Treatment.—This can be divided into two heads: (1) Direct surgical intervention. (2) Surgical intervention with radium.

It cannot be too clearly stated, however, that until the exposure and examination of the primary growth, it is impossible in the majority of cases to say which procedure should be adopted. This fact is of less importance than would appear at first sight, as the initial procedures are similar. The importance of oral sepsis in relation to the ulcerative process has already been pointed out, and this sepsis has a great bearing on the ultimate success of treatment. Those cases which have long been edentulous have a far less stormy convalescence after operation than those with teeth. For this reason it is advisable to delay operative procedure until the teeth have been extracted and the gums are healed. General and local improvement frequently follows this procedure.

Tracheotomy is essential, as this is not only necessary during the operation, but will be required later for a varying period. If the case can be treated by surgery alone, some plastic procedure will be required, and a flap, or flaps, will have to be taken from the anterior part of the neck. A horizontal incision is therefore necessary for the tracheotomy, as the usual vertical incision will interfere with the flap. This is made immediately above the suprasternal notch and tracheotomy is performed, the isthmus of the thyroid gland being divided or partially removed. After exposure of the trachea, cocaine is injected into the lumen, and in place of the usual longitudinal incision a disc is removed large enough to allow a StClair Thomson tracheotomy tube to be inserted. Light chloroform anæsthesia is sufficient for the remaining procedure, and this can be augmented, if necessary, by an injection of morphia.

An incision is then begun just below the angle of the jaw and carried vertically downward to the upper border of the thyroid cartilage where it is carried inwards across the neck of the opposite sterno-mastoid and then vertically downwards to below the level of the cricoid, where it passes back across the neck and is continued downwards towards the clavicle. A flap is thus formed with its base on the side of the neck. The base should be a little wider than the free end.

This flap consists of skin and subcutaneous tissue until the sterno-mastoid is reached. Here the base of the flap should contain sterno-mastoid muscle as well, this last being deliberately divided. The vertical incisions are deepened and a modified gland dissection performed. This dissection includes the internal jugular vein and reaches from the omohyoid below to the digastric above, but does not include the submaxillary triangle.

The carotid vessels are now lying exposed with the stump of the superior thyroid artery. It is advisable to divide this some way from the main vessel in order to minimize the risk of secondary hæmorrhage. Some procedure must then be adopted to shut off the carotids and mediastinum from subsequent sepsis. This can be done either by suturing the remains of the sterno-mastoid to the prevertebral muscles, Trotter's original method, or by turning outwards the pretracheal muscles and the right lobe of the thyroid and suturing them to the sterno-mastoid, the fascia on their lateral and deep aspect being apparently sufficient protection from spreading sepsis after the pharynx is opened. If the latter procedure is adopted, the great cornu of the hyoid, the lateral mass of the thyroid cartilage, and the upper portion of the trachea are exposed.

The thyroid cartilage on the side exposed is now separated and two-thirds of it is removed. Palpation of the primary growth at this time will determine whether it is capable of surgical removal, or whether radium treatment should be adopted. Three points need attention in making this examination: (*a*) the upper limits of the growth; (*b*) involvement of the cricoid; (*c*) the lower limits of the growth.

(*a*) A high upper edge to the growth, within reasonable limits, does not preclude operation. It will have reached a higher level posteriorly than anteriorly, and

although on palpation the posterior upper edge appears to be above the level of the upper opening of the larynx, this does not necessarily mean that the arytenoid cartilages are so involved as to make the case inoperable.

(*b*) Involvement of the cricoid cartilage is usually on the signet portion, but the growth may still be operable. If it has come through on the lateral aspect an advanced condition is indicated.

(*c*) The lower limit of the growth is by far the most important. The post-cricoid growths have a tendency to spread downwards rather than upwards, and this limit of spread cannot be diagnosed beforehand, so that frequently the growth has extended beyond the cervical œsophagus and is inoperable.

Operable Growths.—With a true post-cricoid growth, considered operable, the lower part of the pharynx and the first part of the œsophagus can be mobilized. The pharynx is then opened immediately above the growth, the raw area in the neck being protected. A strip of gauze soaked in cocaine is inserted into the larynx, to anæsthetize it and to prevent blood from running into the trachea. The area involved is then removed by sight. Before the œsophagus is divided across, two retention sutures should be placed in the lower portion to prevent retraction. If a growth does not involve the greater part of the circumference of the hypopharynx it may not be necessary to mobilize the post-cricoid region. There is now a gap in the hypopharynx and a reconstruction has to be undertaken. Sterile boracic powder is placed in the wound and the skin flap is brought forward. Owing to division of the sterno-mastoid, it lies flat in the neck. This flap is sutured, the upper edge to the upper posterior wall of the pharynx and mucous membrane over the arytenoids, and the lower edge to the upper posterior part of the œsophagus. The free edge of the flap is then curled forwards and sewn to the edge of the skin from which it had originally been divided. The upper lateral wall of the pharynx is then sutured to the upper skin edge from which the flap had been taken and the anterior part of the œsophagus to the lower skin edge. There is thus a trough of skin, at the lower end opening into the œsophagus and at the upper end opening into the pharynx. A feeding tube is passed into the œsophagus and left exposed in the neck.

Inoperable Growths.—If the growth is inoperable the pharynx should not be opened, but the case should be treated by radium. There is a choice of either applying radium at once or of waiting for a week to allow the neck to get shut off and so diminish the risk of sepsis. If the gland dissection has been extensive the delay is to be advocated, but if the patient has been edentulous for long and the gland dissection limited, the radium can be inserted at once.

Although the term radium has been used it is found better in carcinoma of the hypopharynx to use radon seeds. These are placed on the outside of the growth so as to radiate the whole area. The seeds are used without threads, first, because the seeds are more easily placed in the position required, and secondly because the presence of threads increases the risk of sepsis, especially when the growth extends down the œsophagus. When the seeds are introduced at once, the flap is resutured, a tube being left in the wound for a few days. If it is decided to leave the introduction to a later date, part only of the flap is sutured, and that portion left which will give best access to the growth. In a week the seeds are implanted, the rest of the wound by that time being sealed off.

If radium element is used it is well to protect the flap by suturing a layer of lead foil between it and the radium; otherwise the flap may suffer severely. The lead foil can be withdrawn with the radium. If radium treatment is employed, a feeding tube should be introduced into the œsophagus by direct vision and brought out of the mouth.

After-treatment.—The tracheotomy tube has to be kept in position until the skin flap has united, or until the radium reaction has settled down.

In cases in which a flap has been introduced a remarkable change slowly appears.

The flap retracts, forming a trough, and later a gutter, so that to look into the bottom of it the sides have to be separated. This can be further accentuated by passing the feeding tube into the œsophagus and bringing it out of the mouth for a few days, and then, under local anæsthesia, incisions are made anteriorly and posteriorly, a tube of skin is fashioned over the feeding tube, and the opposing skin edges left are drawn together.

Untreated carcinoma of the hypopharynx has a hundred per cent. mortality. The mortality of the treated cases is high, and the number that can be eventually claimed as cures is small, but relief can be given in many cases, and with improved diagnosis and increasing experience in technique, the mortality rate will decrease. This has been the experience in other branches of difficult surgical endeavour and will doubtless prove so in the treatment of carcinoma of the hypopharynx.

Lionel Colledge : If a case of post-cricoid carcinoma comes for operation in a tolerably early stage without cord paralysis and without a severe degree of dysphagia, the operation which Mr. Trotter described about twenty years ago is ideal. Our President was kind enough to help me with the case of a lady who came from India in 1927. Mr. Trotter himself saw her with me and urged that the operation should be performed. A complete segment of the hypopharynx was removed and replaced by a flap of skin. She lived at her home near Edinburgh until last year, when, as Mr. Gardiner informs me, she died from mediastinal metastases.

It has been my experience, however, that many patients are sent in a far more advanced stage. One lady arrived from Wales full of hope, but with the larynx and surrounding tissues firmly fixed to the front of the vertebral column, and others come with a severe grade of dysphagia. It is usual to regard the spreading edge of an epithelioma in this region as rising upwards behind the arytenoid cartilages towards the pharynx proper. As Mr. Hunter has emphasized, it also spreads downwards, and on three occasions I have found that in association with severe dysphagia, the growth had spread down the œsophagus through the thoracic opening. In one of these the growth was a simple plaque on the back of the cricoid, but lower down it surrounded the œsophagus forming a long annular stricture.

Severe dysphagia is therefore a sign of ill-omen, apart from its obvious effect on the general nutrition of the patient. There is also another route of extension laterally, through the wall of the hypopharynx, and in this way the posterior border of one or both of the lateral lobes of the thyroid gland may be invaded.

I mention these pathological observations because, in addition to the numerous cases which are obviously unsuitable for operation on account of fixed lymphatic glands, there are others in which the extent of the growth is greater than appears at first sight. Thus many cases are unsuitable for any operation except gastrotomy.

A man, aged 61, was admitted to St. George's Hospital on August 22, 1931. He had noticed dysphagia for two months, and for three weeks had only been able to swallow liquids with great difficulty. The food was felt to stick in the neck. Mr. Fedden performed gastrotomy on August 25, and asked me to see him, having in view the possibility of a radical operation. The right half of the larynx was fixed, a mass could be felt behind the right lateral lobe of the thyroid gland, and a skiagram seemed to show the growth reaching down to the thoracic aperture. I concluded that the growth had extended in both the directions I have mentioned and therefore no operation was attempted.

On September 4, under local anæsthesia, nine radon seeds, each corresponding to 1·5 millicuries, were implanted on each side of the neck. The patient was soon relieved, and now he is able to swallow solid food, no longer uses the gastrostomy, and has gained 14 lb. in weight. I cannot agree with Mr. Hunter, therefore, that an open operation is needed in order to implant radon seeds.

There is, however, an intermediate class of case in which the chief extension is into the posterior wall of the larynx. This invasion of the crico-arytenoideus posticus muscles causes abductor paralysis, not infrequently bilateral, and it may demand tracheotomy. The growth may even perforate the back of the larynx and appear in or near the posterior part of the glottis. It is in this class of case in which I have failed to keep pace with Mr. Trotter, because to remove the septum between the larynx and pharynx and reconstruct it to any large extent by means of a folded skin flap presents difficulties which, I am aware, are not insuperable, but which are of a formidable nature.

In such circumstances, therefore, I have resorted to the operation of Gluck in which the larynx is removed along with a segment of the pharynx containing the growth. The pharynx is re-formed with a double layer of skin flaps, after an interval of from four to six months, and the patient is left in the same state as after a simple laryngectomy. I have shown such a patient here among a group exhibited at the beginning of this year to demonstrate various operations for cancer of the larynx and pharynx. She remains well, swallows easily and is quite active, and she shows that the operation is quite practical. The plastic was performed in one stage and not in a series of operations as Professor von Eicken suggests may be necessary.

The operation of Seiffert, described in the "Handbook" of Denker and Kahler, seems to me a kind of surgical perversion, which sacrifices the functions of the larynx when they might be preserved, and I cannot believe that it will take a permanent place in surgical practice.

The necessity of a bilateral gland operation must be assumed, but it is remarkable how often enlargement of the cervical glands is late in appearing, in spite of the size of the growth. When the glands appear they are often high up under the ears. Leaving the question of glands aside, the present position is, therefore, that in reasonably early cases without vocal cord paralysis, the ideal operation of lateral pharyngotomy with implantation of a skin flap should be employed, and that in more advanced—but still operable cases—the operation of Gluck is justifiable. In cases which are unsuitable for operation but in which the general condition is still fairly good, radon seeds may be implanted with benefit.

StClair Thomson said that he had kept notes of seven cases which he had referred to Mr. Trotter. The important point which he hoped to illustrate was as to which cases were promising and which were not, according to the situation.

The first case which he would quote illustrated the difficulty of diagnosis. Inspection (direct and indirect) and X-ray examination had failed to reveal what he had suspected from the purplish condition of the post-cricoid region and from the froth often to be observed in the sinus pyriformis. At the end of a month the growth became evident and it had the appearance of a sea anemone. It was a post-cricoid epithelioma. At University College Hospital in 1920 Mr. Trotter operated on the case. The operation was a success, but there was a recurrence and the patient died.

The next case was that of a woman from King's College Hospital. There were no enlarged glands in the neck; the movement of the cords was good. Mr. Trotter operated and removed the mass, but the patient had a recurrence in the neck and died eighteen months later.

In another case of post-cricoid growth he, the speaker, had pointed out the froth. There was a recurrence in this case also.

The next case was scarcely eligible for this discussion, as it was one of a growth on the pharyngo-epiglottic fold, but it was worth mentioning because Mr. Trotter had operated from the side of the neck, and the patient had remained well and free from recurrence for six years.

The next case illustrated what Mr. Trotter called the suitable type, viz., growths limited to the aryepiglottic fold. Deep glands were felt, and the cords moved normally. The case was operated upon and promised to be most satisfactory, but

two or three weeks after the operation the patient died unexpectedly from heart failure; he was aged 67.

The next case was the fourth mentioned by Mr. Trotter.

The next case was similar to the foregoing. The patient was aged 66, and was in the habit of imbibing alcohol freely. There were no enlarged glands; one cord showed slight impairment of mobility. Operation was performed in November, 1917. The patient then returned to Scotland and did not appear again until 1922. The cord on the operated side was then fixed, and had a soda-water bottle appearance, due to compensatory hypertrophy. There was no recurrence of disease on the operated side, but a new fresh growth had developed in almost the analogous position on the other side. Mr. Trotter thought the case was again suitable for operation, but the patient went back to Stornoway, had retention of urine and died, aged 71, five years after the operation.

The last case was that of a patient sent to Mr. Trotter from King's College Hospital on account of a similar (aryepiglottic) growth. He had been shown before the Section twice. He had remained well for eight years, and then had a fresh growth on the opposite side, in an inoperable region.

Douglas Harmer: TREATMENT BY RADIOTHERAPY.—In the Semon Lecture (1931) he (the speaker) had quoted statistics collected from twenty clinics about patients treated with radiotherapy. There were 705 cases, and of these, 563 were dead, 101 living. Of the living, 18 were free from disease over two years, one over three years, five over four years, but only seven over five years. 54 other cases were living with disease. For years he and his colleagues had been employing different forms of ray treatment for carcinoma of the hypopharynx. In all they had treated 106 patients, of whom 95 were now dead, only 11 living. 70 died within a year, 23 after a year, one after two years, one after three years; five were living without disease, and six cases living with disease for one to two years. Thus the results from radiotherapy alone, so far, had been bad. That, however, he thought was due to two main factors: (1) that the cases were nearly all hopelessly inoperable: (2) that most of them had not been given adequate dosage. It was useless to send a patient with an extensive growth to the ordinary X-ray specialist who had only a small-current apparatus, under the expectation that any good would result; on the contrary, a small dose was much more likely to do harm.

It would be asked, what was the best treatment for cases of this type. Except in rare instances he did not think it was possible to benefit such cases simply by implanting seeds or radium needles: good results could not be obtained from small amounts of radium; mostly such cases needed combined treatment. First they must receive a surface irradiation, and this must be supplemented so as to get a sufficiently high tissue dose. Patients such as these needed (1) an intense X-ray treatment given from outside, or treatment with a large quantity of radium at not too great a distance; (2) immediately after that treatment, before the growth had had time to recover itself, needles or radium seeds must be buried in the primary growth, or they could be placed in the secondarily enlarged glands.

He had not seen good results follow the insertion of radium needles or seeds from inside the throat, but with careful dissection of the neck, if these growths were exposed freely, without trauma to the tissues around, and particularly to the growth itself, then if radium or radon seeds were applied close to the disease, without opening the pharynx, there was a good chance of getting rid of the growths, at least temporarily. Further research in radiotherapy for this disease was urgently needed. He hoped that by better technique and more thorough irradiation, a large proportion of these patients with inoperable growths would be given relief and in rare cases a brilliant cure might be obtained. In all cases an X-ray examination of the chest should be made before treatment was begun.

Stanford Cade: It is still a matter of difficulty, in any given case, to decide whether excision, radium, or X-radiation, offers the best chance of cure. The difficulty is not lessened by the fact that the term "hypopharynx" is not sufficiently accurate, including, as it does, different types of lesions. A classification of neoplasms in this situation is important; such a classification must include an accurate localization of the growth, as to the origin, position and extent, the histological variety of the tumour and the extent of metastatic involvement.

In cases which are frankly inoperable the choice of treatment is naturally limited to radiation, and the decision as to whether radium or X-rays, or a combination of both, should be advised, depends primarily on the facilities available. If the institution possesses a modern high-voltage machine, X-rays have been shown to be as efficient as radium, provided that the surgeon does not forget that what matters is not only the voltage of the machine, or the quality of the tube, but the man behind it. In experienced hands, high-voltage X-rays used by experts who understand the clinical aspect of the problem and who have the courage of their convictions, good results are obtained in a sufficient number of cases to show beyond doubt that X-radiation has a definite place in the treatment of this group of tumours.

In inoperable cases therefore, X-radiation should be given either as the sole method of treatment or as a preliminary to interstitial radium.

Operable cases present a much more difficult problem. It is convenient to subdivide the hypopharynx into three groups: (1) The epilaryngeal group—the upper part of the hypopharynx; (2) the post-cricoid area—the middle part of the hypopharynx; (3) the pyriform fossa—the lateral part of the hypopharynx.

The first group may be either a squamous-celled carcinoma with cell-nests, or a lympho-epithelioma. The latter, from its very rapid growth, high radio-sensitivity, and early dissemination, is essentially suitable for external irradiation. This group should be submitted to radiation in preference to excision, as the first method of treatment. In the squamous-celled type external radiation is to be followed by insertion of radium on the outer wall of the hypopharynx in close proximity to the growth, but well beyond it in extent; preliminary removal of the thyroid, cricoid, or hyoid skeleton, according to the exact situation of the lesion, is carried out. Needles are preferable to seeds, radium is preferable to radon, and maximum screenage is of the greatest importance. The functional results in successful cases are so superior to anything which excisional surgery can offer, that patients naturally prefer radium. The ultimate expectation of life is not shortened by such treatment.

The second group—post-cricoid area—is of a less radio-sensitive type, presents great difficulties of access and has proved, at least, in my hands, unsuccessful as far as radium is concerned. Should preliminary X-ray treatment not lead to diminution in the size of the growth, excision is to be advocated, provided the whole disease can be removed, the chances of survival reasonable, and the glands not too widely involved.

The third group—pyriform fossa—occupies an intermediate position as regards success in radiation. The disease can be made to disappear in some cases, and this is a sufficient encouragement for continuing research in radiation. Most cases are, at the best, on the borderline of operability and success from surgery is very limited. Radiation should be by means of radium with a preliminary X-ray treatment. The radium should be applied in close proximity to the lesion, either by open operation or by closed needling, later to be supplemented by careful seeding of the primary growth. In this group, so-called "teleradium" or "teletherapy" is on theoretical grounds a method of great promise. The term "tele," however, is, in my opinion, a misnomer, and should be abandoned. It is meant to emphasize the idea of distance which, however, in radiumtherapy is merely an unavoidable difficulty and not a desirable condition. "Mass radiation" is preferable, and applied to the pyriform fossa does produce retrogression of the disease, whereas with teleradium I have so far had no success.

In conclusion, the choice of the method of treatment depends upon localization, extent and type of the disease. Epilaryngeal growths should be treated by radium in preference to surgery, post-cricoid growths by surgery when possible, pyriform fossa growths by radium in split doses with massive quantities of radium. In all cases preliminary X-ray treatment is indicated.

W. M. Mollison said he wished to say a word in favour of deep X-ray therapy for post-cricoid growths. Eight years ago he had seen a patient who had a post-cricoid growth, and he offered her the choice of surgery or deep X-rays. Dr. Finzi carried out the irradiation, and to-day she remained well, and there had been no sign of recurrence.

Since the Deep X-ray Department was set up at Guy's, in charge of Dr. Watt, he had referred all cases of post-cricoid growth there. To-day he showed a woman who, four years ago, came to the hospital with post-cricoid growth. She was unable to swallow anything except fluids—and those only with difficulty. She had been given deep X-ray treatment, and had remained free from recurrence. Two months ago she again developed symptoms and a recurrence is present on the posterior pharyngeal wall above the level of the arytenoids: again a three-day series of deep X-rays had banished the symptoms of pain in the ear and neck, and the growth was smaller.

Admittedly some growths in this region did not respond to deep X-rays, but often they did. He had had three cases of growth in that area, all clinically similar; one responded, but in the other two the patient had soon died, i.e., within three months.

V. E. Negus said the only point he wished to make was the necessity of early diagnosis. He had had the opportunity of seeing one patient who experienced discomfort in swallowing, which was referred to the pyriform sinus. He was examined by the direct method by means of the œsophageal speculum, and small prominences were seen on the lateral wall of the pyriform sinus, which microscopical examination showed to be fibromata with inflammatory infiltration. It was felt that the condition was progressing towards malignant change. He, the speaker, had operated by Mr. Trotter's method, and removed a wide area of the pharyngeal wall by the transthyroid method; the patient had since kept well. There were no malignant changes on examination of the specimen.

A second patient was one whom he was showing at this meeting; she had what seemed to have originated as a fibroma, growing low down on the back of the cricoid cartilage. That was removed by lateral pharyngotomy. That apparently started as a fibroma, with secondary malignant change.

In a third patient there had been an atrophic condition of the mucous membrane of the crico-pharyngeal fold, with secondary anæmia. He had examined this patient over a long period, and at the final stage there were definite malignant changes. The secondary anæmia was severe—only 40% of hæmoglobin—and the patient died.

He emphasized the fact that direct examination was necessary, especially when any discomfort in swallowing was present. Other cases of atrophy and superficial ulceration of the crico-pharyngeal fold could be improved or cured by dilatation and administration of liver extract.

CASES ILLUSTRATIVE OF THE DISCUSSION.

Two Cases of Carcinoma of the Hypopharynx. — E. MUSGRAVE WOODMAN.

(1) R. G., male, aged 59. Admitted to hospital 4.6.26, complaining of dyspnœa, dysphagia and loss of weight. Duration of history, six months. On admission he was thin and cachectic and had a slight inspiratory stridor.

On examination under an anæsthetic, there was seen to be extensive growth involving the left vocal cord, the left arytenoid, the whole of the post-cricoid region and the left lateral wall of the pharynx over a large area, and the upper entrance to the œsophagus.

Complete laryngectomy with partial pharyngectomy 10.6.26.—The sterno-mastoid muscle was stitched down to the prevertebral fascia after the method devised by Mr. Trotter. It was not possible to cover the wound area completely; the remaining part was packed with iodoform gauze and an œsophageal tube passed through the mouth.

Plastic operation.—An attempt was made to close the area by plastic flaps taken from the neck, but there was excessive salivation and on each occasion the wound broke down, and as the area cicatrized considerably, narrowing of the food passage took place, and gave rise to a great deal of trouble. A tube pedicle was taken from the chest-wall by a series of plastic operations and the area covered over.

Criticism.—The criticism of this case is that it is probable that at the initial removal of the growth, the condition of the mouth and of the saliva was too septic and that a sloughing cellulitis caused an additional loss of tissue in the neck. This should have been avoided by allowing a longer interval to take place between the removal of his teeth and the primary operation. Secondly, the isolation of the pharynx and the suture of the muscles of the prevertebral fascia should have been undertaken at a preliminary operation. At present it is possible by plastic work to improve the swallowing considerably, and material in the form of a tube pedicle is in situ ready for this. The patient himself is quite satisfied with his condition and does not wish to have any further operation.

As it is now five years since the first operation, I think he can fairly safely be considered to be out of danger from risk of recurrence.

(2) J. B., aged 49. 29.8.28, admitted with a sudden attack of dyspnœa, following a difficulty in taking solids, and hoarseness. Duration of history, six weeks.

On examination a large mass was found filling the right side of the entrance to the larynx, with sloughs on the surface. The base appeared to originate on the right lateral wall of the pharynx, and the invasion of the larynx to be a secondary extension.

The first operation was a low tracheotomy. The growth was found to have invaded the post-cricoid space, the body of the larynx and the right posterior and lateral wall of the pharynx. The pathological report showed a squamous epithelioma. A complete laryngectomy was performed at a second operation.

Subsequently the patient had a short course of lessons in voice production, so as to utilize the œsophagus as a means of voice production.

12.6.31.—Examination showed the larynx to be completely healed, with no evidence of growth.

20.11.31.—Condition quite satisfactory.

Carcinoma of the Hypopharynx.—F. J. CLEMINSON.

B. B., female, aged 69. Complained of swelling in the throat. On examination a non-ulcerated growth was observed in the posterior third of the right ary-epiglottidean fold.

February, 1926.—Growth removed by lateral pharyngotomy. At the same time the glands of the right side of the neck were removed.

Microscopical examination showed that the growth was a squamous-celled carcinoma, and that there were no secondary deposits in the glands.

Hypopharyngeal Carcinoma treated by Deep X-rays. Freedom from Recurrence for Four Years.—W. M. MOLLISON.

Patient, female, aged 47. Seen at Guy's Hospital in 1927 on account of high degree of dysphagia : ulcerating mass seen projecting from the hypopharynx : condemned as inoperable at a throat hospital. Deep X-ray treatment given by Dr. Watt. Disappearance of growth, and within three weeks, power of swallowing almost normal.

Remained well until 1931 when she had discomfort in throat though no dysphagia. Recurrence on posterior pharyngeal wall above level of arytenoids. More deep X-ray treatment in October, 1931.

Two Cases of Carcinoma of Pyriform Fossa treated by X-rays.—DOUGLAS HARMER.

(1) Female, aged 65. August, 1928, angeiomatous growth removed from the right arytenoid at another hospital. Section reported "squamous-celled carcinoma." Seen in March, 1929, complained of dysphagia, sore throat and pain in head. Right arytenoid swollen but not ulcerated; right cord fixed; small movable gland right side of neck. Mucus in right pyriform fossa. Treated by X-rays from March 19 to 29, 1929. Growth became smaller and she gained 1 stone in weight. In August 1929 growth had not entirely disappeared, so a further course of treatment was given August 25 to September 9. Patient improved slowly and early in 1930 there was no evidence of growth. Weight has been maintained and the throat has remained well, but patient still complains of pain in the head.

(2) Male, aged 65. June 1928. Sore throat and dysphagia for three months; ulcerated growth in right pyriform fossa and arytenoid region; cord fixed; enlarged gland beneath the angle of the right jaw. Treated from June 7 to June 22, 1928; primary growth rapidly disappeared; second treatment from November 8 to 21, 1928, and by January, 1929, gland had disappeared. In December, 1929, he had acute perichondritis, but made a good recovery and remains free from disease.

Two Cases of Carcinoma of Post-cricoid Area.—STANFORD CADE.

(1) E. P., male, aged 49. Admitted to Westminster Hospital in May, 1926. Six months' history of loss of voice, blood-stained sputum, difficulty in swallowing, and marked loss of weight. Extensive malignant growth involving both arytenoids and post-cricoid area. No palpable glands. Complete removal of larynx and of the major portion of the pharynx leaving only a strip of mucosa along the prevertebral area. Immediate repair by means of skin-flap over a rubber tube. Free drainage provided. Histology : Squamous-celled carcinoma.

Recovery. Free from disease to date (5½ years). General health good. Patient has doubled his original weight (from 6½ to 13 st.). Earns his living as a barber. Speaks in a whisper. Is able to eat anything.

(2) M. H., female, aged 46. Admitted to Westminster Hospital in March, 1927. Extensive post-cricoid growth with involvement of lateral pharyngeal wall, thyroid gland and lymphatic glands on the left side. Gastrostomy and tracheotomy performed. Two weeks later, under regional anæsthesia, complete laryngectomy and pharyngectomy, also hemithyroidectomy and removal of cervical glands on left side. Prevertebral muscles covered by skin-flap. Histology : Squamous-celled carcinoma.

Well to date (4½ years). General health greatly improved. Saliva dribbles from submental sinus. Refuses plastic for repair of anterior wall as she is quite content with present condition.

Carcinoma of Lateral Pharyngeal Wall.—STANFORD CADE.

C. D., male, aged 55. Admitted to Westminster Hospital in August, 1928. Epithelioma of left tonsillar area with extensive involvement of lateral pharyngeal wall. Six weeks' history; no palpable cervical glands. Primary lesion treated by

implantation of radon seeds (16 seeds 1·2 millicurie each, screened by ½ mm. platinum). Complete retrogression of the disease. Two months later, block dissection of the left side of the neck. Histological examination showed a deposit of squamous-celled carcinoma in one of the glands. Small local recurrence in region of posterior pillar in June, 1929, treated with diathermy. Well to date (3 years and 3 months).

Carcinoma of Vallecula involving Epiglottis and Lateral Pharyngeal Wall.—STANFORD CADE.

G. F., male, aged 64. Admitted to Westminster Hospital March, 1928. Lateral pharyngotomy for purposes of access only, cervical glands removed. Radium needles inserted (15 mgm. in 8 needles screened by 0·65 mm. of platinum), left in position seven days. Pharynx left open till removal of needles, then allowed to heal; free drainage. Histology: Squamous-celled carcinoma. Two months later, surface irradiation of neck by means of a columbia paste collar: 33 mgm. of radium 15 hours daily for 14 days. Well to date (3½ years).

Carcinoma of Pharyngeal Wall Removed by Lateral Pharyngotomy.—V. E. NEGUS.

The patient was first examined in July, 1929, when an obvious neoplasm was seen on the wall of the pharynx, involving the pharyngo-epiglottic fold and pushing the epiglottis and aryepiglottic fold inwards.

July 15, 1929.—Tracheotomy, under local anæsthesia, followed by lateral pharyngotomy, July 16. The operation was carried out according to the method of Mr. Trotter, the sterno-mastoid being sewn down to the prevertebral fascia after clearance of the local gland area. The growth spread downwards into the upper part of the pyriform fossa; it was excised completely, the area removed including part of the lateral wall, a portion of the aryepiglottic fold, and base of the epiglottis. The wound healed slowly without secondary suture, and the patient has remained quite well for the last two years, his only complaint being some stiffness and pain in the back of the neck.

Microscopical examination showed the growth to be an epithelioma, with a change in some parts to adeno-carcinoma. There was no keratinization, and the microscopical appearances represented a moderately high degree of malignancy.

Sections of a lymphatic gland removed showed inflammatory gland changes, but no evidence of carcinoma.

Carcinoma of Hypopharynx.—V. E. NEGUS.

Patient, female, aged 47 (previously shown April, 1927, and June, 1928).

First seen October 11, 1926, complaining of gradually increasing difficulty in breathing. Symptoms had been present for five years before this date. A hard, rounded neoplasm with slightly irregular surface was seen lying above the larynx, obstructing the airway; it was removed through the mouth by Mr. C. M. Hope, October 13, 1926. A small pedicle remained, arising from half-way down the posterior surface of the cricoid cartilage to the right of the mid-line.

Microscopical examination showed the tumour to be an epithelioma, with very extensive keratinization; there was also much fibromatous tissue present, suggesting that the neoplasm was originally a fibroma, the epithelium of which had undergone malignant changes.

October 28, 1926.—Right lateral pharyngotomy, with local clearance of glands. The growth was found to infiltrate not only the posterior wall of the larynx but also the lateral pharyngeal wall in the pyriform fossa, there being a second pedunculated neoplasm in this region. A considerable area was removed, comprising the mucous

membrane covering the right half of the larynx, together with an almost complete segment of the deep pharynx.

A gap was left between the lower cut edge of the pharyngeal mucous membrane and the top of the œsophagus ; skin-flaps were turned in on November 15, and again on December 20, 1926, but final closure of the gutter so formed was not obtained before March, 1927, the long interval being due to repeated separation of the flaps.

The patient has remained well for the last five years, and swallows with ease.

CASES OF GENERAL LARYNGOLOGICAL INTEREST.

Post-cricoid Papilloma.—R. J. CANN.

Alice P., aged 51. Since Xmas, 1930, has had a sensation of something obstructing her throat, the discomfort being relieved by swallowing.

March 6, 1931.—Examination showed excess of mucus in the hypopharynx and the upper edge of a post-cricoid neoplasm. Two courses of deep X-ray treatment given in March and May, without effect.

October 29, 1931.—Examination under a general anæsthetic showed a sessile growth encircling three-quarters of the lumen of the hypopharynx. The surface was pale, not ulcerated, while the whole mass moved freely.

Two successive biopsies were made and on each occasion Professor Nicholson reported the growth to be a papilloma.

Pharyngeal Ulceration (Bilateral). Case for Diagnosis.—D. F. A. NEILSON.

Patient, male, aged 42. First complained of sore throat and dysphagia twelve months ago. Six months later noticed a lump on the right side of his neck. First seen three months ago.

On examination.—Extensive ulcer on right faucial pillar and smaller ulcer of similar appearance on left anterior pillar ; both ulcers hard to the touch with indurated margins. Wassermann reaction, negative. Skiagram of chest : nothing abnormal. No evidence of tuberculosis. Swab from throat showed staphylococci and streptococci.

Portions of growth from pharynx and from secondary swellings in cervical glands were reported as due to chronic inflammation, and without evidence of malignancy.

During the last six weeks the ulcers have altered very little in appearance. The larynx appears to be normal. Pain and dysphagia still persist. The patient has had several injections of novarsenobillon but there has not been any noticeable improvement.

Discussion.—Mr. E. WATSON-WILLIAMS said that the section of the gland convinced him that this was a case of malignant lymphoma.

Mr. NEILSON, in reply, said that the condition showed improvement in comparison with its appearance when he first saw it in July. Still, he intended to treat it as a malignant case, and apply radium.

Section of Comparative Medicine.

[*November* 25, 1931.]

DISCUSSION ON ACTIVE IMMUNIZATION IN VIRUS DISEASES.

Dr. C. H. Andrewes: In discussing any subject—and perhaps more particularly when discussing viruses—generalizations are dangerous. They are, however, allowable to openers of discussions who wish to set up ninepins for others to bowl at. In this spirit I put forward the following propositions: (1) Our ideal in trying to produce an active immunity against a virus disease must be to induce an immunity as solid and lasting as the dramatically solid immunity which follows a natural attack of most virus diseases. (2) At present we have no methods available which approach this ideal except those by means of which we deliberately produce a mild—perhaps inapparent—attack of the disease. It may be necessary, in order to produce immunity to certain viruses, such as measles, to produce a definite febrile reaction; with other viruses this seems unnecessary. (3) The immunity produced by dead virus—in order to satisfy everybody I will use the convenient term "apparently dead virus"—is comparatively slight and transient. I am not denying that some degree of immunity may be produced by such apparently dead virus; indeed, it may prove useful in helping us one step on the road to the goal of solid and lasting immunity. Formalinized distemper vaccine affords us a good example.

Some people hold that the solid immunity which many virus infections leave behind them is associated with persisting latent infection with virus. I do not agree nor do I disagree with the view; there is not available enough evidence to let us decide the point. Clearly, however, those who hold such a view will not expect to find a persisting immunity without the use of a method of immunization involving the injection of living virus.

Mild, abortive, or inapparent infections may be induced as a means of immunization in several ways. (1) We may inoculate an attenuated virus. Such virus we may find ready-made, like vaccinia, or we may be able to produce it in a stable form by animal passage as we do with rabies fixed virus. (2) More often we are not so fortunate—the thing is not so easy. We then have to attain our end by inoculating fully virulent virus into a partially immune animal. We may give our animal a low degree of passive immunity by inoculating virus and serum at the same time, as in side-to-side methods—or we may bestow a small degree of active immunity by means of a previous inoculation of apparently killed (e.g., formalinized) virus.

In some instances the method of immunizing with serum+virus only works if serum and virus are given by the "side-to-side" technique on opposite sides of the animal—as in dog-distemper and rinderpest; the serum must not act on the virus outside the body. In other instances, such as yellow fever, and perhaps vaccinia, a serum-virus mixture can apparently be used. Possibly the difference depends upon some such factor as this: distemper immune serum may rapidly form a stable union with the virus so that no infection at all results. Yellow fever virus and its antibody may unite more slowly or the union may readily dissociate within the body so that the net result is much the same as if the two had been injected separately.

It is of some interest to inquire how one is able, with a side-to-side inoculation or with live virus following up formalinized vaccine, to induce a very mild disease. It might be thought that if there was any multiplication of virus at all, as we believe there is, the partial immunity of the animal would be presently overcome and the complete disease would blossom out. But this seems not to happen. Possibly the partial immunity (active or passive) restrains the virus-multiplication in its early stages or confines it locally; active immunity begins to develop, or to increase, right from the start and is already at a useful height before much virus spills over into

the blood-stream. Experiments which I performed with neurovaccine support the suggestion that after a side-to-side inoculation active immunity may be developed very quickly, even within twenty-four hours.

This neurovaccine, when given intravenously to rabbits in large doses, invariably induced a generalized eruption of pocks on the skin. 3 c.c. of antiserum intravenously could protect against 3,000 minimal infective skin doses, given intravenously—that is, could prevent generalization. Rabbits 3 and 4 in the table show that this dose failed to protect against 200,000 m.i.d. intravenously. Rabbit 2 shows

	Treatment		Test:	
Rabbit	Virus intradermal	Serum intravenous	Virus intravenous	Generalization
1	60,000 m.i.d.	nil	200,000 m.i.d.	+
2	60,000 m.i.d.	3 c.c.	nil	0
3	nil	3 c c.	200,000 m.i.d.	+
4	nil	3 c.c.	200,000 m.i.d.	+
5	60,000 m.i.d.	3 c.c.	200,000 m.i.d.	0
6	60,000 m.i.d.	3 c.c.	40,000 m.i.d.	0

that this dose, 3 c.c. given intravenously, could also prevent generalization from resulting after a large dose of virus given intradermally. So much for controls; now for the experimental animals. Two rabbits were given a side-to-side inoculation, a dose of virus into the skin of one ear and 3 c.c. serum intravenously to the opposite ear. Twenty-four hours later they received a large dose of virus intravenously; they completely failed to show generalized lesions. Now rabbits 3 and 4 show that they could not have had enough passive immunity to stop generalization after this big dose of virus, from which I deduce that their active immunity had already reached a considerable degree of usefulness after twenty-four hours. This experiment has been carried out four times in all, with the same result each time. I think it has some bearing on the mechanism by which side-to-side inoculations may produce only a mild disease.

I alluded to the possibility that immune animals may be immune because they are persistent virus-carriers. If we aim at immunizing by giving a mild disease, may not we be running a risk of making a lot of virus carriers? Waldmann, Trautwein and Pyl[1] have been able, by concentrating virus on charcoal, to find foot-and-mouth virus in the urine of a hyperimmunized ox 246 days after its last inoculation. I am told that in America it is recognized that once immunization against swine fever is started on a farm, it is disastrous to stop immunizing in subsequent years; the very fact of previous vaccination seems to increase the danger. Such facts should make us wonder whether we might not spread a disease by vaccination in a country where it does not already exist. Probably our vaccination will usually confer a disease so extremely mild that there is no danger at all. But if very many animals are being vaccinated, some will be sure to respond abnormally and may develop a disease not so mild, capable of infecting others. Even if there is a remote risk such as I have indicated, I think it need not deter us to-day from actively vaccinating against a widespread disease like dog-distemper. One would, however, hesitate to vaccinate in this country against foot-and-mouth disease. In conclusion, I would plead for more experimentation on the lines suggested by the work of Waldmann, Trautwein and Pyl.

Professor W. Tulloch: In this discussion I am merely the spokesman of Dr. James Craigie, now of the University of Toronto, who, although introduced to the study of the serology of vaccinia by myself, has achieved far more than I could hope to do. I take this opportunity of paying tribute to his energy, his loyalty and his ability.

1 *Cent. Bakt.*, 1 O , 1931, 121, 1?.

So far as our joint work on the application of serological methods to the study of vaccinia virus is concerned, the findings may be summarized thus:—

(1) The diagnostic value of the vaccinia flocculation test and its specificity appear to be proved.

HUMAN MATERIAL.	Number	Result
Smallpox Minor	106	POS
" Major	14	"
Varicella	67	NEG
Other Skin Conditions	6	"
Human Vaccinia	7	POS
Material Unsatisfactory	3	?
MATERIAL OTHER THAN HUMAN.		
Vaccine Lymph	4	POS
Lapine	30	"
Caveine	6	"
Natural Cowpox	2	"
TOTAL	245	
Experimental Error	1·23%	

A

(2) The reaction is not due to there being present in the antigen adventitious antibodies to secondarily infecting bacteria.

Anti-Vaccinia Serum 'F2' Prepared by Immunising a Rabbit with 'STERILE' Material from the Same Species.						
Antigens for	Dilutions of Extracts.					
Flocculation	1/500	1/1000	1/2000	1/4000	1/8000	1/16000
Dermal Lapine	x	xxx	xxxx	xxxx	xx	x
Smallpox	—	x	xxx	xxx	x	—
Control NORMAL Rabbit Serum						
Dermal Lapine	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—
Serum Dilution CONSTANT for Both 1 in 40						

B

(3) Antiserum, such as is used for conducting the flocculation test, contains antibodies possessing anti-infective quality in high degree.

Ref. No. of Rabbit.	Antivaccinia 'Y' Flocculating Serum. 2 c.c. per Kilo Intravenous.	Infecting inocula.	Dilutions of Infecting Inocula. Degree of Reaction. Inoculation by Scarification.					
			1/500	1/2500	1/10,000	1/50,000	1/250,000	1/1,000,000
XN3	18 Hours before Inoculation.	K2	0	0	0	0	0	0
		M3	0	0	0	0	0	0
		N2	0	0	0	0	0	0
XO3	1 Hour before Inoculation.	K2	0	0	0	0	0	0
		M3	0	0	0	0	0	0
		N2	0	0	0	0	0	0
XP3	Normal Rabbit Serum-Control 18 Hrs. before	K2	IIII	IIII	IIII	III	II	I
		M3	IIII	IIII	IIII	III	II	I
		N2	IIII	IIII	IIII	III	I	0

C

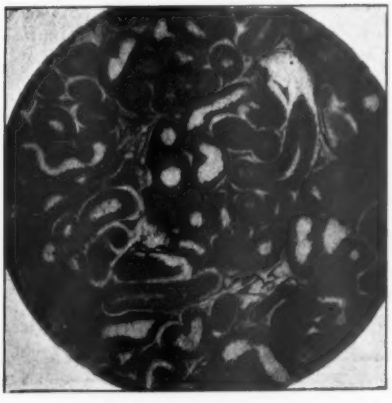


FIG. 1.—Testis inoculated with virus but having previously received flocculating serum.

(4) The precipitate obtained by flocculating extracts of vaccinia material with such antiserum contains vaccinia virus. The virus thus treated is, however, peculiar in that—

(*a*) Its infectivity is much diminished.

Infecting Inocula Administered Intradermally.	Dilutions of Infecting Inocula. & Degree of Reaction.							
	$\frac{1}{25}$	$\frac{1}{100}$	$\frac{1}{500}$	$\frac{1}{2500}$	$\frac{1}{10,000}$	$\frac{1}{50,000}$	$\frac{1}{250,000}$	$\frac{1}{1,000,000}$
UNTREATED Vaccinia Extract.	IIII	IIII	IIII	IIII	III	III	I	O
'SENSITISED' Vaccinia Extract.	O	O	O	O	O	O	O	O

D

(*b*) It does contain living virus, as is readily shown by intra-testicular inoculation of the virus thus sensitized.

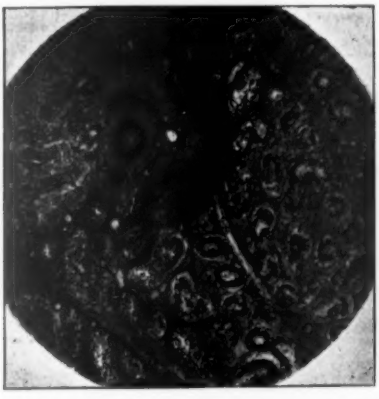


FIG. 2.—Testis of rabbit inoculated with sensitized virus.

(*c*) It stimulates the production of immunity.

Ref. No. of Rabbit.	Immunising Inoculum of 'SENSITISED' VIRUS.	Interval between Immunisation & Test.	Infecting Inocula.	Dilutions of Infecting Inocula. Degree of Reaction. Inoculation by Scarification.						
				$\frac{1}{25}$	$\frac{1}{100}$	$\frac{1}{500}$	$\frac{1}{2500}$	$\frac{1}{10,000}$	$\frac{1}{50,000}$	$\frac{1}{250,000}$
XO4	.041g.	11 Days	W3	O	O	O	O	O	O	O
			M4	O	O	O	O	O	O	O
XP4	.041g.	9 Days	W3	III	III	III	I	O	O	O
			M4	III	III	III	III	III	I	O
XQ4	.041g.	5 Days	W3	IIII	IIII	IIII	IIII	IIII	II	O
			M4	IIII	IIII	IIII	IIII	IIII	II	O
XR4	.041g.	2 Days	W3	IIII	IIII	IIII	IIII	II	I	O
			M4	IIII	IIII	IIII	IIII	III	I	O
XS4	Control-NIL		W3	IIII	IIII	IIII	IIII	III	I	O
			M4	IIII	IIII	IIII	IIII	IIII	III	O
Same Result Obtained using .0001g. for Rabbits of 2 Kilos.										

E

The technique of the work upon which these statements are made, and the significance of the last observation in relation to the production of an immunizing inoculum devoid of, or at least with reduced, danger either of undue local reactions or of untoward sequelæ, have already been discussed fully in a recent publication.

I therefore propose to deal with further investigations which we have made, as these break new ground in virus research.

We have been careful never to commit ourselves as to whether the flocculated material did, or did not, represent virus precipitated by its appropriate antiserum.

It is possible to separate extracts of vaccinia material into two moieties, one of which is markedly flocculable and of low infectivity, while the other is not readily flocculable but is highly infective.

This separation can be achieved in more than one way. The easiest method is to filter suitably prepared extracts of the material through a Seitz E.K. disc, then having washed the disc to remove any flocculable substance contained within it, to reverse the disc and, washing in the reverse direction, obtain by this procedure the following: (1) filtrate which is flocculable but not infective; and (2) the material washed from the filter by reversing the fluid current, which product is infective but not markedly flocculable.

Ref.	FLOCCULABILITY.				INFECTIVITY.			
No.	Control	Filtrate	Last Wash	Residue	Control	Filtrate	Last Wash	Residue
125	1/8000	1/4000	1/625	1/125	1/2,500,000	< 1/25	< 1/25	1/2,500,000
130	1/16,000	1/16,000	1/250	1/125	1/25,000,000	< 1/25	< 1/25	1/2,500,000
135	1/16,000	1/4000	not done	1/500	1/50,000,000	< 1/50	< 1/50	1/5,000,000

F

Sometimes it is necessary to use double disc filtration in order to obtain filtrates that are proved to be devoid of infectivity when tested by intratesticular inoculation. We are therefore forced to ask ourselves the question, What is flocculable substance? It may be the product of the living virus, a product of the dead virus, a product of the invaded tissue or a combination of these. One is tempted to suggest that its relation to the virus might be akin to the relation existing between pneumococci and their specific carbohydrates.

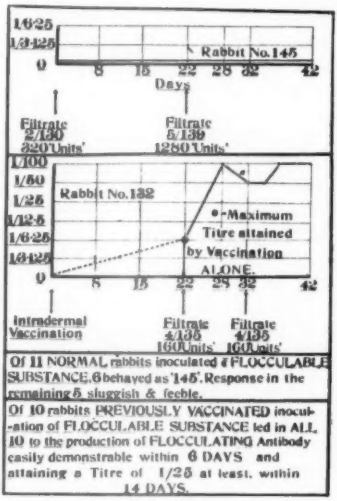
A partial answer to this question may be given if we can answer another question, namely, What are the antigenic qualities of flocculable substance? In this connection the following experiments have been done.—

(*a*) Flocculable substance—i.e., non-infective filtrate—when inoculated into normal rabbits may fail to stimulate the production of flocculating antibody. If flocculating antibody should appear (remember that absolute separation may not have been achieved) the response is sluggish and feeble. (See G and H, upper section.)

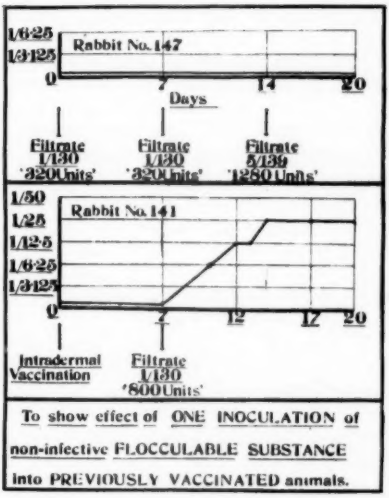
(*b*) Flocculable substance—i.e., non-infective filtrate—inoculated into rabbits that have previously been vaccinated by dermal vaccination alone, gives rise to a prompt and marked development of flocculating antibody. (See G and H, lower section.)

The term "unit" used in these charts is, of course, purely arbitrary but, for purposes of comparison, it was necessary to establish some kind of base line. The unit of flocculable substance is that amount of flocculable substance contained in a

volume of 0·5 c.c. of the highest dilution giving definite flocculation with an antiserum, chosen at random, and used as a standard throughout one series of experiments. For example, if a rabbit received 1 c.c. of a filtrate equivalent to a dilution of lapine of $\frac{1}{20}$ and the flocculating titre of that lapine extract in 0·5 c.c. volume is $\frac{1}{16000}$, the number of units given would be $\frac{16000}{20} \times 2$, that is, 1,600 units.


1/625
1/3125
Rabbit No. 145
0
8 15 22 28 32 42
Days
Filtrate 2/130 320 Units'
Filtrate 5/139 1280 Units'
1/100
1/50
1/25
1/12·5
1/6·25
1/3125
Rabbit No. 132
•-Maximum Titre attained by Vaccination ALONE.
0
8 15 22 28 32 42
Intradermal Vaccination
Filtrate 4/136 1600 Units'
Filtrate 4/136 1600 units'
Of 11 NORMAL rabbits inoculated with FLOCCULABLE SUBSTANCE, 6 behaved as '145'. Response in the remaining 5 sluggish & feeble.
Of 10 rabbits PREVIOUSLY VACCINATED inoculation of FLOCCULABLE SUBSTANCE led in ALL 10 to the production of FLOCCULATING Antibody easily demonstrable within 6 DAYS and attaining a Titre of 1/25 at least, within 14 DAYS.

G



H

The findings shown in G and H, upper sections, suggest that the flocculable substance is *not* antigenic, but that is in direct contradiction to the findings shown in the lower sections of the same slides, which do indicate that it serves as a secondary stimulus.

How are we to explain the anomaly? It is possible that the filtrate contains living virus in quantities sufficient to act as a secondary stimulus but insufficient to act as a primary stimulus. This suggestion seems to me to be susceptible to criticism in view of the large doses of the material used.

If we attempt any other explanation of this direct contradiction, two significant points emerge:—

(1) That a material which fails to act as a primary stimulus may perfectly well act as a secondary stimulus to the production of antibodies—a somewhat novel finding in immunology; and (2) There is so close an association between flocculable substance and virus that it looks as though flocculable substance were a product of the virus living or dead.

The implication of these findings in relation to the further study of virus diseases and immunity thereto is obvious, but perhaps the most interesting observation of all is contained in a letter just sent to me by Dr. Craigie. He has shown that flocculable filtrates proved by testicular inoculation to be free from virus, when inoculated into humans who have already been immunized by ordinary vaccination, lead to an early and very severe response.

Major G. W. Dunkin. *Active Immunity to Dog Distemper.*—A dog which has recovered from a natural attack of distemper, that is to say the virus disease, appears to be immune to further attacks. The immunity resulting from such an

attack is probably durable and life-long in the vast majority of cases; to such an extent, in fact, that it can be considered to be the rule. There are a few exceptions to this rule and instances have been recorded where a second or even a third attack has occurred. It is by no means clear, in view of the confusion which still exists as to what are the cardinal symptoms of the disease, and of the admitted difficulties experienced in diagnosis, whether these reported recurrences are in fact true distemper or some bacterial infection the symptoms of which closely resemble those of true or virus distemper.

Active and durable immunity frequently follows a natural attack of a virus disease, e.g., swine fever, but it cannot be said that the immunity resulting from a natural attack of this disease is as lasting as in the case of distemper, for the reason that as a rule a pig does not live as long as the average dog. On the other hand, an attack of foot-and-mouth disease does not appear to confer any lasting immunity—as far as natural attacks in the field are concerned. The difference in the degree of immunity resulting from attacks of swine fever and dog distemper on the one hand, and of foot-and-mouth disease on the other, is probably explained by the fact that in the latter case one has to deal with more than one strain of virus which does not appear to be a factor to be considered in the case of either dog distemper or swine fever. As far as has been possible to ascertain and as a result of work conducted on some twenty or more strains of dog distemper virus, it has been found that all these cross immunize.

In the case of dog distemper the immune state may be established in dogs and ferrets without any great risk to the animal, in a number of different ways. Formalized and carbolized as well as heated virus have all been used as vaccines. Although encouraging results have been obtained from all these methods, the most successful results have been obtained by the use of formalized virus and this method is the one in general use to-day.

(*a*) The immunity conferred by the injection of vaccine alone is certainly not lasting. Two doses injected at an interval of a week or a fortnight result in an immunity of longer duration than that conferred by one dose, but in any case it is evanescent.

(*b*) Vaccine followed by living virus, the latter given at a certain interval after the vaccine, produces an immunity which is active and durable. In order to attain this end, the virus used must be living and virulent and it will naturally follow that if this is to be so, then the vaccine must be of known high protective power, otherwise an attack of distemper is almost certain to result and may terminate fatally. Both products must, in fact, be beyond suspicion.

(*c*) The simultaneous serum-virus method. This method has been more recently employed, and while it possesses certain obvious advantages over the former and the resultant immunity appears to be good, the time which has elapsed since its inauguration is insufficient to allow one to state with certainty that it is durable. The method adopted is the side-to-side injection of the two products and, as in the case of vaccine and virus, both products must be of known and high value.

(*d*) Mixtures of serum and virus injected into susceptible animals either subsequent to or without incubation have invariably proved disappointing. The method, in so far as dog distemper is concerned, is useless.

(*e*) Virus which is stored in the moist or semi-dry condition gives some interesting results. There appears to be a stage in its degradation when it will fail to reproduce the disease but will act as an efficient antigen. It is not possible to say exactly how long it takes before this stage is reached, because the time varies with different samples of virus and even with the same virus on different occasions. The critical period is of short duration but its exact time limit is unknown, and while this phenomenon is of considerable scientific interest, if not importance, as a general method of immunization it is not a practical one, for the antigenic power of the virus

must be tested on animals before it can be issued, and by the time the result of the test is known the antigenic power may have disappeared.

This is reminiscent of the preparation of Pasteur's dried rabies virus and it will be recalled that by exsiccation a gradation of the immunizing material—although inexact—was possible; inexact for the reason that the spinal cord is not equally impregnated by virus in all its parts, and also because the varying thickness of the cord, with an even period of drying, results in a more or less drastic reduction of the organism.

(*f*) Sub-infective doses of distemper virus known to be living and virulent do not appear to be of any value in producing resistance to the disease. Multiple doses have not been tried.

A point of considerable importance in connection with immunization against dog distemper is that the "vaccine" is highly specific for species. In other words, "dog" vaccine, although of the greatest value in the protection of dogs, will fail to protect ferrets unless it be given in multiple doses. The converse is equally true; that is, "ferret" vaccine, although good for ferrets, will not protect dogs in single doses. One therefore naturally wonders whether or not ferret vaccine would be of any value as a prophylactic for such valuable fur-bearing animals belonging to the same species as the mink and fisher, or whether dog vaccine is to be of any value when used on, say, silver foxes.

Rudolf, in Vienna, has described distemper in the mink, silver fox and also in the racoon. Hinz in Berlin, in a personal communication, and Wood in America have confirmed these observations in so far as mink are concerned. Dalling in this country has described dog distemper in the fitch and this is confirmed in a personal communication received from Law in Ontario. These valuable observations adding, as they do, to the number of species alleged to be affected by dog distemper, suggest to one's mind that, as the vast majority of fur-bearing animals belong either to the Mustelideæ or to the Canideæ (the racoon cannot, of course, be included in either of these categories) it should be possible to immunize them by means of one or other of the methods just briefly described.

The nature of the immune state, resulting either from a natural attack or produced by artificial means, provides much ground for conjecture. Is the immunity due to the persistence of the specific antibodies in the animal system, to the constant stimulation of the antibody factory by the admission of virus received as a result of frequent contacts with "open" cases of the disease, or is it due to the persistence of living virus in the animal system which by its presence causes a constant stimulus to the manufacture of fresh antibody?

The correct explanation is not clear, but in view of the fact that the administration of virus must take some place in securing active and durable immunity, the explanation probably lies in the suggestion that living virus persists in the tissues of the immune animal which thus becomes a perpetual carrier of the disease. It must be admitted that there is a complete absence of evidence in support of this contention in the case of dog distemper and all attempts to isolate the virus from recovered or immunized animals, even from those which have been suspected of being carriers, have failed. None the less it appears on the whole to be the most satisfactory explanation of the life-long immunity observed in this disease.

Dr. S. P. Bedson said that in immunization against virus diseases our ideal should be the production of the maximum degree of immunity with the minimum degree of danger or discomfort. The method of prophylactic vaccination against smallpox at present in vogue hardly achieved this ideal and an endeavour should be made to devise a better method. The experiments which Professor Tulloch had described held out the hope that we might find our ideal

method along the lines of immunization with neutral serum-virus mixtures. The method of immunization which consisted of inoculating the unprepared animal with a fixed relatively avirulent variant, the classical example of which was Jennerian vaccination, was only of limited application, and for protective inoculation against the great majority of virus infections we had to choose between immunization with living virus in a partially immunized animal or immunization with dead virus alone. In the former method partial immunity might be achieved either passively by means of an antiserum or actively by means of killed virus, the choice of method being determined by the virus with which one was immunizing and the animal species to be immunized. For example, it would appear to be extremely difficult to produce a reasonably potent serum against the virus of psittacosis and in a case like this one would have to rely on a dead vaccine for the production of partial immunity. With regard to dead vaccines it was usually stated and generally accepted that all filtrable viruses when killed were equally good—or bad—immunizing agents. His experiences did not lead him to this conclusion. He had worked with three viruses from this point of view, the virus of foot-and-mouth disease, herpes virus and psittacosis virus; and his colleague, Dr. Bland, had experimented with vaccinia virus. And whereas killed vaccinia virus provoked little or no immunity, the virus of foot-and-mouth disease and herpes gave quite effective killed vaccines, and killed psittacosis virus produced as good an immunity as that conferred by an attack of the disease. Mice when infected with psittacosis, usually died, but those that recovered had only acquired a moderate degree of immunity, yet by means of formalinized virus alone it had been found possible to produce quite a high degree of immunity in this animal. Dr. Andrewes was of the opinion that it was a waste of time to discuss whether a filtrable virus that was really killed had the power to provoke immunity. Personally he (Dr. Bedson) disagreed with this, for apart from the purely academic interest attaching to this question there was a practical one. If the antigenic activity of the "killed" vaccines was due to partially inactivated virus, then their efficacy was likely to be ephemeral and it was going to be difficult to know with certainty when, and for how long, a vaccine could be expected to be effective, whereas if its efficacy was due to killed virus we could hope for a much more stable product. Experiments which he had carried out with herpes virus did not support the view that the antigenic power of a formalinized herpes vaccine was due either to a residue of active virus or to attenuation of the virus; it appeared that herpes virus that was really killed could give rise to quite a high degree of immunity. In conclusion, he would like to put in a plea for further research on immunization with killed virus.

Mr. R. E. Glover: Generally speaking, the most satisfactory results in the active immunization of animals seem to have been obtained with combinations of serum with virus (serum-simultaneous methods: sensitized virus), and these methods are still holding their own. Nevertheless, the obvious drawbacks, such as the difficulty of obtaining adequate supplies of fully potent virus and the dangers of creating fresh centres of infection with the inoculum, have stimulated enquiries into methods which are safer, but are still capable of giving a durable immunity.

The most promising results seem to have been obtained by the use of an inert vaccine, either alone (e.g., rinderpest), or followed by a reinforcing inoculation of fully virulent material (e.g., distemper). The latter method is open to the objection that at some stage of the immunizing process the animal may be capable of spreading the disease. On the whole, it must be admitted that the results obtained with inert emulsions have been disappointing. With a single dose of killed virus, the immunity is only partial and is extremely fleeting; with two or more doses, a solid protection can be induced, but it is usually of comparatively short duration. These points are illustrated by experiments with fowl-pox. Such methods are unlikely to be of

value in the lower animals, because on economic grounds, repeated inoculations are rarely possible.

It is necessary to determine whether phenol, formalin, etc., produce an attenuation of a virus, or whether there is a progressive lethal action. Experiments with fowl-pox indicate that the latter obtains, and that the residual virus is fully virulent. It is suggested that a point is reached at which the amount of virus which is left is insufficient to set up the disease, but is still capable of immunizing: at a latter stage, the virus is entirely destroyed, and is then antigenically inert. This may explain the discrepant results which have been obtained in many virus diseases.

Dr. Mervyn Gordon said that it was desirable to have more information as to what viruses were, and of the manner in which they acted. Evidence was accumulating to show that they were minute living organisms (e.g. the recent work at the National Institute on the mouse disease, and of Ledingham on the Paschen bodies in vaccinia and variola). In the case of vaccinia it was easy to show by titrating measured dilutions on the rabbit's skin that the greater part of this virus did not pass through filters such as the Berkefeld, L_2, or Seitz, and microscopical examination revealed the presence of these very small but definite bodies that seemed to be the actual agent. In the case both of vaccinia and psittacosis he (the speaker) had found no evidence of the presence of soluble toxin, and it seemed probable, therefore, that these viruses acted by means of the endotoxin contained within the bodies of the minute organisms concerned. Confirmatory evidence of this had been obtained in case of vaccinia in course of some experiments he had made with a view to determining the nature of the protective substance in anti-vaccinia serum. The addition of active guinea-pig complement to vaccinia virus in presence of normal serum increased its pathological action on the rabbit's skin and gave rise to necrosis. This necrotic effect was neutralized by a very potent anti-vaccinia serum, but not by others, and he thought that pointed to the action of anti-endotoxin.

We knew that a virus, such as vaccinia, excited the production of specific antibodies (e.g., complement-fixing antibodies and agglutinins), very much as ordinary bacteria do. Further work at these larger viruses would probably prove fruitful because if we knew more about them we should be better able to deal with the smaller and more difficult viruses.

Dr. Wilson Smith said that his work on vaccinia during the last eighteen months had been along lines similar to those discussed by Professor Tulloch. His results suggested that this virus might have a complex antigenic structure. He had extracted from vaccinal rabbits' testes a substance which gave a specific precipitin reaction with vaccinia immune sera. This substance would withstand boiling, so that there could be no question of the survival of any living virus. It had failed entirely to provoke an immunity response in rabbits subjected to multiple inoculations over a period of six months. It was conceivable therefore that this heat-stable precipitating body was of the nature of a haptene, analogous to the specific soluble substances derived from pneumococci and, if so, it might assume importance as a non-living immunizing agent if it could be made antigenically active by linkage to a protein.

Professor G. H. Wooldridge said that one point of considerable clinical importance had not been stressed sufficiently in the course of the discussion, namely, the possible infectivity of the vaccinated subject during the period of developing active immunity. Dr. Andrewes had suggested that in the case of dog distemper it was not of much importance, owing to the ubiquitous distribution of "street"

distemper. He, the speaker, thought, however, that it assumed great importance in the case of animals inoculated with virus in hospitals, because if they eliminated virus after inoculation they must inevitably be a source of danger to other susceptible dogs in that hospital. Was there any really definite information on this point? His practice was to isolate or segregate inoculated dogs for a week or ten days after injection of virus. He did not think that there was any likelihood of vaccinated dogs becoming carriers, and he had never had any reason to suspect the existence of the carrier in dog distemper—the position in this respect differing clearly from swine fever, in which the existence of apparently healthy carriers was well established.

Section of Anæsthetics.

[*December* 4, 1931.]

Resuscitation during Anæsthesia and of the Newly-born.

By Sir Francis E. Shipway, K.C.V.O., M.D.

It is fitting and proper, indeed essential, that this Section should consider the subject of resuscitation from time to time, for anæsthesia is a pathological process which involves the abolition of sensations and reflexes; the means whereby it is produced necessitate also the production of paralysis in varying degrees. Anæsthesia is not sleep, but a state of unconsciousness brought about by the action of depressing drugs or conditions; at times there must be a danger of paralysis of the respiration and the circulation. The restoration of these vital processes is resuscitation. The fact must be recognized that the administration of an anæsthetic is a scientific and complex proceeding, which may demand more skill and entail greater responsibility than the performance of the operation. It must also be recognized that there are desperate conditions aggravated by the shock of surgical interference which may be beyond the capacity of the anæsthetist to bring to a successful issue. But whilst this statement can be justified it must be conceded that many deaths are preventible; accidents arise partly from lack of proper knowledge of methods of resuscitation, and partly from delay in their application.

Resuscitation may be defined briefly as the restoration of the nervous and muscular activities of the body. These activities depend largely upon an adequate supply of oxygen and the removal of any excess of carbon dioxide. The exchange of gases may be interrupted in the following ways: (1) temporary paralysis of the nervous system owing to lack of oxygen or the action of anæsthetics; (2) paralysis of the muscles of respiration, generally secondary to paralysis of the nervous centres; (3) failure of the circulation of the blood.

Arrest of breathing may be due to mechanical obstruction, paralytic causes, or a combination of these. The airway may become inadequate owing, for example, to spasm of muscles, swelling, excessive secretion, the presence of a foreign body, or interference with lung expansion. Paralytic arrest of respiration may arise from (*a*) toxic effects, such as an overdose of anæsthetic, or (*b*) anoxæmic condition due to an insufficient supply of arterial blood caused by shock, change of posture, or the influence of the anæsthetic on the cardio-vascular system. Failure of the circulation may be primary, dependent upon, for example, change of posture, overdose, fibrillation, or secondary to embarrassed or arrested breathing.

Artificial respiration will supply the needs of the nervous system and reduce the amount of the anæsthetic which is depressing the nervous centre; further, the alternate expansion and contraction of the lungs produce a mechanical effect by pumping the blood, and a respiratory reflex if the medulla is excitable. This is the Hering-Breuer phenomenon, in which each expiration causes an inspiration. If the medulla has been paralysed by lack of oxygen or excess of carbon dioxide, this phenomenon can no longer be obtained by artificial respiration alone. The

sensitivity of the respiratory centre in the medulla has been decreased and its threshold for carbon dioxide raised. It can, however, be increased and the threshold lowered to normal by an increase in the amount of carbon dioxide in the inspired air. This is quickly accomplished by artificial respiration combined with the administration of oxygen and of sufficient carbon dioxide to stimulate the centre.

The treatment of respiratory paralysis due to the action of drugs, volatile or non-volatile, which depress the centre is upon similar lines. If respiration has become very shallow, oxygen alone is insufficient to supply the needs of the nervous system. As early as 1910 Levi used mixtures of carbon dioxide and oxygen for the purpose of stimulating the centre in cases in which the effects of anæsthetics, of operative shock, or a combination of these causes had temporarily paralysed its activity. He obtained the best results with a mixture containing 15% carbon dioxide, and administered it on the appearance of the slightest tendency to failure of respiration or circulation. He recognized clearly the importance of prevention of the onset of respiratory collapse.

Henderson and Drinker, at the Centenary Meeting of the British Association for the Advancement of Science, stated that as a result of their wide experience in the resuscitation of newly-born children and of persons suffering from carbon monoxide asphyxia, a percentage of 7 was often found to be effective when one of 5 had failed. In some cases a percentage of 8, or even 10, was needed to stimulate an asphyxiated respiratory centre. It is clear that for the mixture of 5% or 6% carbon dioxide in oxygen commonly used in this country, one containing at least 7% should be substituted, and a cylinder containing a mixture of this strength should be available in every operating theatre. Too much emphasis can hardly be laid upon the value of carbon dioxide for resuscitation. It is the natural stimulus of the respiratory centre, is easy to give, and more effective than artificial respiration. Further, it exerts a powerful influence upon the tonus of the skeletal muscles and thus, by augmenting the venous return to the heart, improves the circulation.

Care must be taken when using mixtures stronger than 10%. A percentage of about 30 produces narcosis and death.

The importance of having available a supply of carbon dioxide occurred in my practice during an operation for the removal of tonsils. The patient was elderly and had suffered for many years from a severe degree of myocardial degeneration. During enucleation under ether and oxygen, the airway being completely free, the respiration began rapidly to fail, and the radial pulse could no longer be felt. The head was lowered and the chest squeezed, but the pupils continued to dilate. Carbon dioxide from the portable sparklet apparatus suggested by Dr. Whitridge Davies was then given whilst artificial respiration was continued, and almost immediately the breathing returned and the condition improved so rapidly that it was possible to complete the operation. This case demonstrates the value of carbon dioxide in restoring the circulation under most unfavourable conditions, and it is highly probable that its prompt use will reduce the number of cases in which a fatal result has ensued in spite of what may be described as the more elaborate methods of resuscitation. Stress may well be laid here again upon the preventive teaching of Levi.

In children resuscitation should present no difficulties. Failure of respiration is best treated by lowering of the head or partial inversion, and rhythmical compression of the chest, combined with the administration of carbon dioxide and oxygen. In the adult Sylvester's method often fails to restore the respiration; the method gives inadequate ventilation, for during the inspiratory movement the diaphragm is elevated, and during the expiratory movement it is depressed. It is particularly inadequate in the obese and the elderly, and it is very fatiguing if continued for more than a few minutes. Howard's method is more efficient and less fatiguing.

The prone-posture method of Schäfer produces the fullest ventilation of the lungs, and is the official method of resuscitation from asphyxia due to drowning or other causes in nearly all parts of the world. Unfortunately it is seldom applicable during an operation, as in the vast majority of cases it entails turning the patient into the prone posture, and imperils asepsis. Moreover, should it fail in restoring respiration and heart-beat and should some form of cardiac stimulation prove to be necessary, still further delay would arise. On the other hand, Schäfer's method can be performed by one person, it removes obstruction caused by the relaxed jaw muscles and tongue, and allows free drainage of mucus or fluids which may have gained access to the air passages. Its use, therefore, should be borne in mind in the event of acute respiratory obstruction arising under anæsthesia and dependent upon the presence of a foreign body. It is hardly necessary to point out that occasions may arise on which laryngotomy or tracheotomy may have to be performed and air forced into the lungs by inflation. Caution must be exercised against the use of undue violence during the performance of any of these methods of artificial respiration, for many cases of fractured ribs and of damage to internal organs have been reported.

Should the heart have ceased to beat, attempts to revive it must be made by massage, intra-cardiac injection of a drug, or puncture of the auricle or ventricle. Massage has been practised for many years. Its function is to stimulate the heart muscle by creating an artificial circulation in the coronary arteries, and to supply the central nervous system with blood. The route which is commonly employed is the subdiaphragmatic, and the heart is either rubbed or kneaded. Many successful cases have been reported. At a meeting of this Section in 1919, Daly, Powell, Apperly and myself reported cases, all of which I venture to think afford valuable lessons. Unfortunately, the majority of attempts at resuscitation by this method are unsuccessful. The route does not give good access, except perhaps in the case of the child, as only the apex is reached, and the heart tends to slip away from the hand in spite of counter-pressure by the other hand upon the chest. Bost restored the heart's action after subdiaphragmatic massage had failed, by incising the diaphragm, passing his hand into the left pleural cavity, and grasping and squeezing the heart. Coleman succeeded in producing a response by this method after subdiaphragmatic massage for half an hour had failed to elicit a beat. He states that the heart "could not be grasped or moved at all through the diaphragm because it was small . . . and lying against the back of the chest wall." Norbury was unable to restore cardiac pulsation in 13 out of a total of 16 cases of subdiaphragmatic massage deliberately performed.

The movements of the hands when the heart is directly grasped are those of compression and not of massage; they effect two purposes, stimulation of the heart by pressure on the nerve ganglia at the base, and emptying of the ventricles, the blood being thereby propelled with more force and efficiency than by the subdiaphragmatic method. In order to prevent pneumothorax the parts are pressed round the wrist. Levy suggests that to prevent this risk whilst artificial respiration is being carried on, perflation of the lungs should be carried out, either by intubation or by the passage of an intratracheal catheter through which a controlled stream of oxygen is passed.

The rate of kneading or of compression should not exceed 30 or 40 to the minute, as the heart usually recovers but slowly in the case of an overdose, the first beats being feeble; there must be brief intermissions to allow it to recover. The first beats are as a rule not only feeble but irregular, and as a regular rhythm may not be established immediately, the heart should be stimulated from time to time until the beats become strong and regular. Petty has reported a case in which the heart failed within a few seconds after massage had produced a response; it was necessary to restart massage and continue it for another minute. Most observers are agreed upon the necessity of continuing massage at intervals until the maximal contraction

has been obtained. The appearance of spontaneous beats may be much delayed. In a case reported by Ogilvie, massage was continued for 75 minutes before they could be obtained.

Artificial respiration must be maintained throughout until natural breathing is resumed. Success has been occasionally obtained without artificial respiration, but it is desirable to ensure the circulation of oxygenated blood.

Intra-cardiac injection of a drug has been frequently practised. Some authors advocate intra-pericardial, some intra-muscular injection; others insist upon the importance of placing the drug into the cavity of one of the ventricles, with a view to its rapid propagation through the blood-stream. It would seem, however, that the rationale of injection into a cavity disappears if the movement of blood has ceased; the amount injected, usually 1 c.c., is too small to be effective. A review of the literature reveals the fact that a correct aim is difficult; the right ventricle has often been punctured in an attempt to reach the left. V. de Velden found, post-mortem, that the usual result of his attempt to reach a cavity was the injection of the drug into the muscle. Bodon and others recommend puncture in the fourth left intercostal space close to the sternal border; the heart is most safely and easily reached by this route.

Many drugs have been used for injection: caffeine, camphor, digitalis, strychnine, strophanthin, adrenalin, pituitrin, metrazol, sodium thiosulphate. Bolton restored pulsation after cardiac arrest under ether by the injection of ether. Imerman revived an elderly patient who was moribund from insulin hypoglycæmia by the injection of a 20% dextrose solution; recovery was immediate.

Adrenalin is the drug advocated strongly by the physiologists. It stimulates the muscle of the heart by its action upon the sympathetic neuro-muscular junction. Gunn has shown that the mammalian heart, arrested by chloroform, can be restored by perfusion with adrenalin. It produces also a temporary rise in the blood-pressure which assists the recovery of the vaso-motor centre and the heart. He has suggested that in the case of arrested action in man the effect of adrenalin can be obtained by its injection into the external jugular vein, combined with cardiac massage. The artificial circulation produced by massage will force the solution "in time" to the heart. The injection of adrenalin has been much advocated and often practised by both physicians and surgeons. It would not, however, appear to be without danger. Johnson and Siebert, repeating the work of Fleisher and Loeb, have shown that myocarditis can be produced in rabbits by intravenous injection of adrenalin. Smirnow states that histological examination of the heart of dogs given intravenous adrenalin during chloroform anæsthesia showed marked destructive changes in the bundle of His. Cleghorn and also Crile state that the injection of adrenalin into a cavity or into the muscle may produce fibrillary contractions.

It would seem unwise also to inject it when chloroform has been administered, owing to its tendency to cause fibrillation in the presence of this anæsthetic. In making this statement I am aware of the view advanced by Levy that adrenalin is not dangerous in the presence of deep chloroform anæsthesia, but only in the initial stages and during recovery from this anæsthetic. The experience of Jones contradicts this view; there can be no doubt that in his cases anæsthesia was of a depth which Levy has pronounced safe. Robinson and Bredeck state that strophanthin also predisposes the heart to fibrillation.

Since success has been attained with each of the drugs already mentioned, the question arises whether the result is due to the drug. Grave doubt must present itself if the problem is looked at in this way. It would appear as if the evidence that the clinician has to offer is convincing. There must be something more than the effect of the drugs, which are numerous and widely different in their actions, which has produced a response from the arrested heart, more particularly as arrest

has usually been caused by the depressant action of chloroform. Is it possible that this "something more" is the mechanical stimulation of the muscle? Watson demonstrated in 1887, in twenty-two out of a total of sixty experiments on dogs killed by chloroform, that puncture alone of the heart was sufficient to start the beat. Some observers have noted a movement of the needle as it entered the heart. Bodon looks upon this as a good augury of success.

Glover, in reporting a successful case of resuscitation by massage, has suggested that the mere prick of a needle may be sufficient to restart the heart. Hyman, acting upon the view that the success of intra-cardiac injection depends upon the irritant action of the puncture rather than upon any specific action of the drugs, succeeded in reviving a patient, who had collapsed during ether anæsthesia, by puncture of the ventricle after all other methods had failed. He states that the arrested heart tends to become irritable and responds readily to any strong stimulus. The first beats are extra-systoles, which are usually succeeded by normal rhythm, but if the myocardium has suffered much damage during the period of anoxæmia arrhythmia may persist and develop rapidly into ventricular fibrillation. He suggests that the onset of ventricular fibrillation is the explanation of a secondary collapse after successful resuscitation.

Extra-systoles arising in the auricles, followed by auricular fibrillation, do not connote collapse or death; the condition is compatible with life. Further, the auricles are known to be more sensitive to stimulation than the ventricles. Reasoning upon these lines, Hyman punctured the auricle in four cases of patients who had died from various diseases. In two the results were successful, the heart-beat being restored in one for a period of seventeen minutes after complete standstill for nine minutes, and in the other, a case of mitral stenosis, for a period of eight days. Hyman has now collected [1] forty-four cases in which auricular puncture has been performed. Four come within Meyer's Group I, the healthy asystolic heart. Two of these responded to this treatment, and are alive to-day. "The third case died about four hours after the heart was resuscitated, and the fourth case died about one hour after resuscitation from hæmorrhage as the result of a compound fractured femur." Of the cases in Group II, i.e., hearts affected by local or general disease, eleven responded to auricular puncture.

To puncture the right auricle a slightly curved needle, 5 in. long, is inserted in the third right intercostal space close to the border of the sternum; it is directed downwards and towards the middle line. In children the auricle lies within about 2 in. of the anterior surface of the sternum; in adults the depth varies from $3\frac{1}{2}$ to $4\frac{1}{2}$ in.

Perhaps the most weighty reason for the large number of reported failures is delay in starting resuscitation. Failure does not arise because of inability to restart the heart-beat, although this is sometimes difficult. It is known that the beat may be restored after many hours of cardiac immobility; the heart retains its irritability and excitability for a prolonged period. By means of perfusion, Gunn has started the beat of an exsected heart of a stillborn child four hours after it was born. It was shown many years ago that the heart of a dog could be revived by massage after being placed in snow for as long as 18 hours. Failure arises because of damage done to the cortical cells through the prolonged interference with their oxygen supply. It is difficult to state exactly how long the central nervous system can be deprived of blood without death of its tissues, but for practical purposes it is more than probable that if the beat has not been restored within five minutes, systemic death will almost certainly occur. Cases of successful resuscitation after periods of apparent standstill of 10, 11, even 14 minutes' duration have been reported. The time of cardiac arrest, however, is difficult to determine with exactitude; the absence of

1 Personal communication, November 11, 1931.

pulse and the impossibility of hearing the heart-beat do not necessarily mean that its action has ceased. Doubt must often arise, and a healthy scepticism must be preserved when reading accounts of resuscitation after a prolonged period of cardiac arrest. On the other hand, some observers have definitely stated that the heart was found to be still and flaccid when palpated through the diaphragm, and it is clear that in other cases the appearance of the patient and the complete disappearance of muscular tone were good evidence of suspended cardiac function. Whatever the facts may be, the conclusion is irresistible that the patient must be given the benefit of the doubt, and that unnecessary delay in taking active measures to restore an effective circulation must be avoided, especially if chloroform has been used or the myocardium is known to be degenerated. Norbury found, in contradistinction to the unsatisfactory results of the delay of opening the abdomen in order to reach the heart, that immediate massage when the abdomen was open was quickly followed in several cases by restoration of the heart's activity. Since the resuscitation of patients moribund from some grave condition such as toxæmia or hæmorrhage seldom meets with a favourable result, there is no object in prolonging attempts in these cases.

In Petty's case of resuscitation after arrest of $6\frac{3}{4}$ minutes, recovery was marked by somnolence lasting for 12 hours; in others, consciousness has never been regained, although respiration and circulation were restored for a considerable time. The case reported by Mollison to this Section in 1916 also enforces the lesson of the danger of prolonged interference with the cerebral blood-supply. The patient, a child, recovered after a period of cessation of the heart's action of at least 13 minutes, and probably longer, but the subsequent history showed that serious damage had been caused to the cortical cells. Symptoms of cerebral irritation continued for about two weeks, the child being unconscious during most of that time and being incontinent; he made subsequently a perfect recovery, but remained below the school standard for two years after the operation. Mollison states that for some moments after starting cardiac massage "there was no response, then some respiratory movements began and continued intermittently; the boy's colour improved and pupils contracted . . . still there was no attempt at heart-contraction." He suggests that this attempt at respiration was due to the slight artificial circulation produced, blood being driven to the medulla and stimulating the respiratory centre. This observation of his, and a similar observation by Fisher, agree with the statement of Gunn that, for the purpose of deciding whether the cells of the central nervous system are capable of complete restoration or not, the time can be calculated, not as from the start of spontaneous heart-beats, but as from the time of beginning massage. It must be remembered in this connection that massage, to be effective, must drive blood to the central nervous system. Proof of success in this direction is given by improvement in the colour and by contraction of the pupils.

Primary circulatory arrest due to ventricular fibrillation arises occasionally during light chloroform anæsthesia. This condition is entirely different from that of overdosage; it must be recognized at once, for the treatment is simple and effective if applied at once. Levy holds that the vast majority of fatalities during the early stage of chloroform administration are caused by ventricular fibrillation. This is not the occasion on which to discuss this much-debated question, but my own experience derived from many thousand administrations, personal or supervised, of chloroform or a mixture containing chloroform, leads me to think that Levy has overstated his case. The only occasion on which I have seen primary cardiac syncope due to ventricular fibrillation was towards the end of an operation, and as the details of these cases are of value they are given here:—

A tall, overgrown youth of 18 had been under chloroform for about thirty minutes for an operation on the nose; the anæsthesia had been of a medium depth and uneventful, circulation and respiration being satisfactory, although not strong. Towards the end of the

operation the concentration of the vapour was diminished and the anæsthetic finally stopped, to prepare the patient for the removal of his tonsils. This case occurred in the days when the opinion was held that such an operation was more safely performed under very light anæsthesia. The first tonsil was removed by the guillotine; at this stage respiration was vigorous and a strong corneal reflex was present. The guillotine was then applied to the second tonsil, but during the course of avulsion the colour, which had been good, suddenly became pale, the pupils dilated widely, and three deep respirations of a gasping character and of succeeding weakness were taken. Respiration then ceased. The sequence of events, namely, sudden cardiac failure followed rapidly by respiratory failure, was so clear that the condition was recognized. The head was immediately lowered, and the chest squeezed vigorously. The pupils soon became smaller, and recovery was prompt.

Jones has reported three cases in which recovery followed very quickly upon inversion.

The outstanding feature in these cases is sudden pallor. Death is obviously not preceded by respiratory failure. The heart has failed not because it is overdosed, but because fibrillation has been produced. There is a spontaneous tendency for it to recover, but it is advisable not to wait too long for this to occur, for if the heart has become asphyxiated it can only be revived by direct massage.

Sir Bernard Spilsbury has allowed me to use the notes of the following case:—

Young man, 27 years of age. Good general health. Chloroform given for removal of tonsils.

Operation had been completed when he suddenly became cyanosed and respiration ceased. Pulse could not be felt at the wrist.

Artificial respiration was commenced at once and the surgeon opened the abdomen and massaged the heart through the diaphragm, and later incised the diaphragm and squeezed the heart.

It was estimated that cardiac massage was started not more than two minutes after the patient became cyanosed.

The heart was flaccid when it was handled at first, but about twenty minutes later it regained its tone. Ten minutes later the ventricle began to fibrillate and it continued to do so until about fifty-five minutes after manipulation of the heart had been commenced, when it suddenly began to beat normally and powerfully and continued to do so for twenty-four hours, when it failed finally.

The patient's colour improved as soon as massage was commenced and remained good until death. Natural breathing did not recommence and artificial respiration was maintained for the whole twenty-four hours. The patient also remained deeply unconscious throughout that time.

Post-mortem examination.—Brain congested. Heart cavities dilated. Muscle showed fatty degeneration microscopically. The manipulation of the heart had produced slight bruising of the outer surface of the left ventricle with a tear on the inner surface to which two small thrombi were attached. There was fatty degeneration of the liver. Thymus gland present and weighed ½ oz. Lymph follicles enlarged in the small intestine.

The case would appear to me to be one of ventricular fibrillation. The signs are not identical in these cases, but the prominent sign is the suddenness of the circulatory failure. Cyanosis may be present, instead of pallor, on account of some slight difficulty with respiration, either during induction of anæsthesia, the cause being holding of the breath, or during recovery, the cause being the act of vomiting. If the sequence of events is closely observed it will be found that the pulse has disappeared before respiration has ceased. These cases which I have quoted illustrate well: (1) the importance of (*a*) correct diagnosis, (*b*) prompt treatment by inversion, and (2) the difficulty of restoring the heart-beat if treatment is not at once successful.

The nervous system and heart of a child apparently stillborn are more resistant to lack of oxygen and excess of carbon dioxide than is the case in the adult. Its lungs resemble a solid organ, and require inflating with air. The first essential before endeavouring to resuscitate a child suffering from asphyxia neonatorum,

therefore, is to clear the air passages of fluid; pulmonary respiration can then usually be established. Fluid is best removed by means of posture or by suction. Mouth-to-mouth inflation supplies sufficient oxygen and carbon dioxide if it is successful in filling the lungs with air, but it is more likely to inflate the stomach. Its use should be reserved for emergencies. Following the clearing of the air passages, the treatment differs according to the type of asphyxia from which the child is suffering. If blue asphyxia is present resuscitation should be easy, owing to the vigour of the circulation. As warmth increases the metabolism and the excitability of the nervous system the child should be laid in a warm place and time given to it to start spontaneous breathing. Should this be delayed, cutaneous stimulation by cold water may be practised. It is erroneous to suppose that stimulation of the skin by douching is all-important; whether the child is born in arctic or tropical regions the tendency is towards spontaneous respiration. If douching fails, or if the heart-beat becomes feeble, artificial respiration by the method of Schäfer should be started.

In the case of a child suffering from white asphyxia it has to be remembered that the circulation is failing. The hold upon life of such an infant is feeble, and extreme gentleness in handling it is essential. Warmth is even more important than in the case of the blue child; gentle artificial respiration and, if it is available, the administration of a mixture of oxygen and carbon dioxide may meet with a favourable response. If these fail in establishing respiration and the pulse becomes more feeble, direct stimulation of the heart by auricular puncture should be attempted.

In some cases white asphyxia is dependent not upon an injury and interference with the placental circulation during a difficult labour, but upon absorption from the mother's blood of a drug which has been used to diminish the pains of child-birth. Morphia and hyoscine are often used to induce the condition known as twilight sleep; chloroform is also frequently given for a prolonged period during labour. These drugs depress the respiratory centre both of the mother and of the child, with the undeniable result that the lives of some infants are endangered, for the resuscitation of a child born under these conditions may tax to the full the resources of the practitioner and his assistant at a time when the demands of the mother upon their services may be imperative. To meet this emergency a mixture of oxygen and carbon dioxide should always be carried, or Davies's portable carbon dioxide apparatus.

To sum up:—

(1) There are many causes of respiratory and circulatory failure.

(2) The use of carbon dioxide and oxygen, both for their prevention, and, combined with artificial respiration, for their treatment is to be encouraged. A supply of this mixture should be at hand in all operating theatres.

(3) Effective ventilation must be maintained both during anæsthesia and during resuscitation.

(4) Partial inversion is of value in the absence of asphyxia; it should be adopted at once for the treatment of primary circulatory syncope.

(5) If the action of the heart cannot be restored by these means, puncture of the auricle followed if necessary by direct massage should be performed.

(6) If the abdomen is already open subdiaphragmatic massage may be carried out; if not successful within two minutes direct massage must be undertaken. Artificial respiration must be maintained throughout until natural breathing is restored.

(7) The time-factor is all-important. Circulation must be restored within five minutes of the time of arrest. The risk of sepsis incurred in opening the abdomen without preparation is to be ignored. If the objection is raised that this is a desperate remedy the answer is that death is a desperate state.

(8) In the infant suffering from blue asphyxia, resuscitation is to be effected by clearing the air passages, and warmth and carbon dioxide and oxygen; in the case of white asphyxia, by gentleness, warmth, and artificial respiration by Schäfer's method combined with the use of carbon dioxide and oxygen.

(9) During all attempts at resuscitation the body temperature of the patient must be maintained.

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Discussion.—Dame LOUISE MCILROY expressed much interest in the description of the treatment of asphyxia in the newly-born as she had devoted some years to researches upon the subject. In the case of blue asphyxia, little anxiety was, as a rule, felt, as respiration became established, in most cases, as soon as the air passages were cleared of mucus. She employed a mucus catheter made from an ordinary rubber catheter and a part of a laboratory pipette. It was better than the metal instrument as the rubber could not damage the infant's mouth, and the glass bulb stemmed the passage of mucus before it reached the operator's mouth. Mucus could be sucked out of the mouth but insufflation was never employed owing to the risk of undue pressure, and also of sepsis, from the breath. The tube for suction was inserted in the infant's mouth, but it was not possible to insert it in its trachea.

In the case of failure in the establishment of respiration she applied a mixture of oxygen 95% and carbon dioxide 5% by means of a mask attached to a pressure-gauge water valve and cylinder. The amount of pressure was most important (8 in. of water) and such a gauge should always be used. Various forms of the apparatus were now used in the Obstetrical Unit of the Royal Free Hospital, the latest device being one which was fixed in the labour ward in a cupboard. It was now absolutely fool-proof and could be used by students or nurses. A portable apparatus was used in the case of the district patients.

Asphyxia in some cases was caused by the first breath of the infant drawing in mucus or liquor amnii. A number of infants born alive required considerable effort in reviving owing to want of precaution in clearing out the mouth.

In her opinion, an infant should be kept warm immediately after delivery. No baths should be given and it should be cleansed with olive oil until separation of the cord had taken place. Artificial respiration, with the exception of gentle compression of the chest and tongue traction, should be entirely superseded by the administration of oxygen and carbon dioxide. Intracranial injury was the most frequent cause of white asphyxia. No adult suffering from similar accidental injuries would be treated with baths or by any method but the most complete rest attainable.

Mr. H. H. KENSHOLE described a case in which cardiac action ceased during the induction stage of chloroform and ether anæsthesia, preparatory to dental extractions.

By cardiac massage trans-diaphragmatically and the administration of oxygen and carbon dioxide (5%) natural respiration had been maintained for two hours, and even after a further two hours with artificial respiration the patient's pupils could be made to contract and his colour markedly to return by recommencing the above measures after withholding them for 30-40 seconds at a time. He (the speaker) asked when, under similar circumstances, an anæsthetist was justified in giving up hope?

In view of the teaching of textbooks for dental students that dilatation of the anal sphincter was by reflex stimulation a potent method of cardiac resuscitation, would Sir Francis express his opinion upon the value of this procedure?

It appeared to him (the speaker) that puncture of the auricle by means of a needle acted

physiologically by stimulation of the sino-auricular node or of the bundle of His; if this were so, would not puncture of either auricle be equally efficacious as that of the right atrium only?

Dr. R. J. MINNITT said that a youth operated upon at the Liverpool Royal Infirmary for a very enlarged thyroid had been given an intratracheal gas oxygen ether anæsthetic from a McKesson machine. Part of the thyroid weighing 1 lb. 1 oz. was removed satisfactorily. At the end of the operation the catheter was withdrawn from the trachea, and soon after the patient showed signs of distress—cyanosis and expiratory dyspnœa being extreme. A gag in the mouth and the pulling forward of the tongue gave no relief. A mixture of about 5% carbon dioxide in oxygen was given for a short time at intervals of fifteen minutes for about an hour. The colour and breathing definitely improved after each administration. When the patient regained consciousness there was no more trouble, and he made an uninterrupted recovery. Dr. Minnitt thought the cause was collapse of the trachea.

Mr. C. LANGTON HEWER said that he doubted whether in "mouth-to-mouth" artificial respiration, much air passed into the stomach. In adults, at any rate, practically no leakage occurred, as could be demonstrated at any time by using considerable positive pressure in a face-piece when the abdomen was open. No dilatation of the stomach could be produced in these circumstances. Probably the most efficient form of artificial respiration was to pass one large rubber intubation tube filling the glottis, and to connect this to a bag and expiratory valve as in rebreathing intubation anæsthesia. The lungs could then be rhythmically inflated and deflated with a carbon dioxide-oxygen mixture, the intrapulmonary pressure being practically equal to that inside the bag.

Mr. I. W. MAGILL said definite establishment of a free air-way appeared to be of first importance, as some degree of respiratory obstruction was not infrequent in cases of respiratory failure during anæsthesia. This was best treated by direct-vision intubation. A laryngoscope and a catheter, or rubber tube for the purpose should be at hand in every operating theatre, as had long been the custom with the tracheotomy set. His experience of intubation in patients of all ages covered some fourteen years and he had not yet observed the untoward results referred to by a previous speaker. When intubation had been performed after respiratory arrest, it was not sufficient simply to blow oxygen into the trachea. Using low pressure, the normal rhythm of respiration should be simulated. During the inspiratory phase the outlet should be obstructed by holding the nose and covering the mouth, thereby ensuring inflation of the lungs. During the expiratory phase the obstruction should be released and the ribs compressed. Continuous high pressure was unlikely to assist pulmonary circulation.

He referred to an apparatus seen at the Mayo Clinic which carried out artificial respiration automatically. It provided alternating positive and negative intrapulmonary pressure and could be regulated to deliver any predetermined volume of air or oxygen-carbon dioxide mixture. The negative pressure phase was held to be particularly important in assisting pulmonary circulation.

In emergencies carbon dioxide could be obtained from an ordinary soda-water syphon. All that was necessary was to invert a full syphon, the gas being released by pressure on the stopcock with the syphon in this position.

Mr. H. E. G. BOYLE related the details of a case in which sudden collapse occurred in an adult patient during a mastoid operation under chloroform, after adrenalin had been poured into the wound to stop the bleeding.

Sir FRANCIS SHIPWAY (in reply) said he thought that dilating the anal sphincter would be of little value in the treatment of serious overdosage. The right auricle was easily reached by the route described in the paper. Cases of scabbard-trachea were rare. He gave the details of one which occurred many years ago, in which it had been necessary to re-insert the catheter after the patient had returned to the ward; the catheter was removed before consciousness had been regained, breathing again became embarrassed and was only relieved by again passing the catheter. Haldane, Henderson, and other physiologists had strongly condemned artificial respiration apparatus which depended upon pressure and suction. The case mentioned by Mr. Boyle illustrated the danger of the combination of chloroform and adrenalin, and reinforced the lesson which he (the speaker) had endeavoured to drive home.

Section of Ophthalmology.

(*November* 13, 1931)

Early Sarcoma of the Choroid.—HUMPHREY NEAME, F.R.C.S.

Micropsia and Central Colour Defect.—Mrs. B. P., aged 50. Two years ago the patient noticed on a particular day on waking that the print on a medicine bottle seen with the left eye appeared smaller than when seen with the right eye. At the same time she noticed that the colour of a bunch of coreopsis seen with the left eye was paler than as seen by the right. The period of definite failure of vision is uncertain.

Glasses prescribed in 1919 for distance were:

R. $\frac{-0{\cdot}75 \text{ sph.}}{-0{\cdot}75 \text{ cyl. axis } 90^\circ}$ L. $-1{\cdot}0$ sph.

31.10.31.—With own glasses (believed to have been prescribed in March or April, 1931):

V.R. $\frac{\text{c.}-1{\cdot}5 \text{ sph.}}{-0{\cdot}5 \text{ cyl. axis } 90^\circ} = \frac{6}{5}$ (mostly).

V.L. Finger-counting at $\frac{1}{2}$ metre; not improved.
Has been wearing L. $+ 0{\cdot}5$ cyl. axis 180°.

Development of Hypermetropia.—Retinoscopy revealed about + 3 D. of hypermetropia.

Examination of the left fundus oculi shows a smooth oval swelling in the macular area projecting into the vitreous by about 3 dioptres. Its nasal border is about 2 d.d. from the disc and it extends laterally 4 to 5 d.d. Many vessels are seen indistinctly on its surface deep to the retinal vessels. The retina appears to be separate from the mass at the upper and nasal margins—that is, not part of it. (This excludes the possibility of a retinal cyst of the internuclear layer). The retina shows faint foldings and striation as of tension between the disc and the growth and to a slight extent above. Faint irregular pigmentation is seen on the lower surface of the swelling. The mass has a solid appearance and shows no movement on turning of the eye.

Postscript (13.12.31).—Swelling now 6 to 8 D.

? Tuberculosis of Lachrymal and Accessory Lachrymal Gland.—JOHN FOSTER, F.R.C.S.

L. C., male, aged 11, was admitted six weeks ago to the Royal Westminster Ophthalmic Hospital under Mr. Hine, as a case of acute dacryoadenitis, following a blow on the eye with a tennis ball a week previously. Pus was evacuated (no culture) but the swelling persisted, and a second swelling appeared in the lower lid two weeks ago. As both swellings exhibited a focal reaction when a Pirquet test was carried out, the above diagnosis is suggested.

I am indebted to Mr. Hine for his permission to show this case.

Discussion.—THE PRESIDENT said that the question whether this was tuberculous or not was still unproven; he did not think the Pirquet test was sufficient. To be conclusive it was necessary to inject into a guinea-pig some material from the upper swelling. He had never seen a tuberculous lid without an enlarged pre-auricular gland. The focal reaction might have been coincident, not dependent on the Pirquet test.

Mr. J. H. FISHER said that in view of the history of an accident, it was not impossible that a particle of foreign matter, e.g. a small splinter of wood, was embedded in the anterior and outer part of the orbit, and that the sinus might be found to lead down to such particle. Mysterious foreign bodies did get into the orbit. It might have gone through the conjunctival surface, or through the skin without any aperture having been observed. He advocated making a semicircular incision round the outer canthus, laying it open, and exploring for a foreign body. If it proved, after all, to be tuberculous, curetting could be done and might prove of advantage. It might be caries of bone. It was not, he thought, the lachrymal gland which was causing the trouble.

Mr. HUMPHREY NEAME said that if this swelling was from the lachrymal gland, it would be more likely to point into the fornix than into the skin. There was, in fact, a swelling on the conjunctival surface of the lid, but the swelling projecting externally was against its being lachrymal.

A Worm-like Structure in the Anterior Chamber.—M. S. MAYOU, F.R.C.S.

W. T., male, aged 69, an old soldier, came to the Central London Ophthalmic Hospital, May 8, 1931, because he had difficulty in reading. Vision, right $\frac{6}{6}$; left, hand movements.

History.—He was hit in the left eye at Gallipoli with a piece of explosive shell. He received no treatment and did not visit the dressing station.

Present condition.—On examination a scar could be seen in the cornea to which the iris was adherent and there was also an opacity in the lens, but the whole of the lens was not opaque. X-ray examination showed that there was no metal foreign

Worm-like structure in anterior chamber. (Mr. Mayou's case.) The tail-end tapers more to a point than is shown in the drawing. The head-end shows small excrescences.

body in the eye. Lying on the iris, downwards and outwards, there was a peculiar worm-like structure which had the appearance of a head at the pupillary margin and tapered off to a tail at the periphery of the anterior chamber. It was pinkish in colour and with a white reflex on the surface. It was strongly suggestive of a dead worm, the sheath of which was tending to become calcareous, probably carried in at the time of the injury.

I know that worms in tissues do become calcareous, but that fact does not necessarily apply to the anterior chamber, because, though the whole posterior part of the uveal tract may be solid with calcified material, the iris never calcifies. I had a talk about it with Professor Leiper, and since then I am beginning to doubt whether it is a worm; perhaps he will tell us why. I know of no pathological condition of things which will give rise to this appearance.

Discussion.—Professor R. T. LEIPER said that the worm might have been present before the accident, and have become involved in scar tissue. It was unusual to find parasites in the anterior chamber of the eye, and none of the recorded cases of the kind had been fully studied by medical zoologists. He felt doubtful about this case. On inspection with a hand-lens the structure bore a close resemblance to a nematode worm; but the photograph suggested that one end of the worm was coiled on itself; and it seemed to have certain knobs on it. This was against its being a nematode. Worms had been described as occurring in the anterior chamber of the eyes of horses, but their life-history involved a biting insect. This patient might have been bitten by an infected insect while he was in the south of Europe, but that implied that the damage to the eye was not related to the sudden occurrence of the worm in the eye. He was puzzled by the involvement of both ends of the worm.

Cataract in an Acetone Worker.—M. S. MAYOU, F.R.C.S.

G.T., male, aged 18½, a paint sprayer. Attended the Central London Ophthalmic Hospital, August 4, 1931, complaining that his vision had been blurred for the last seven weeks. Vision: R. eye, barely, hand movements; L. eye, $\frac{6}{9}$. The right lens is completely cataractous. It was of the very soft flocculent snowflaked type such as is usually associated with diabetes. The left eye shows commencing lens changes, especially in the subcapsular region. Urine sp. gr. 1022; contained no sugar or albumin. Blood sugar, examined on September 8, 1931, was 0·137%. Patient was admitted to the Central London Ophthalmic Hospital, October 18, 1931. There was then no sugar or acetone in the urine and the blood sugar was normal. The carbohydrate tolerance was normal. On October 20 the right lens was needled. No further operation has been done since that time. The question arises as to the possibility of the acetone causing the cataract, since acetone is also present in diabetes, a disease associated with similar changes in the lens.

If acetone is the cause, the patient must have an idiosyncrasy for this poison. I put the case on record in case other instances arise in the painting trade.

Discussion.—The PRESIDENT said there was so much cellulose painting of motor cars, the paint having been dissolved in acetone, that if it had an influence on the occurrence of cataract there would probably be many more cases, especially as the workers were shut up to keep the air away.

Mr. F. A. WILLIAMSON-NOBLE said one would expect this condition to occur when there was acetone in the breath. A brother of his had periodic attacks of acidosis, and he was noted to have a posterior polar lens cataract. He was not diabetic.

Mr. A. GRIFFITH asked whether it would not be truer to say that the appearance was typical of toxic cataract. Appearances precisely similar to this were found in toxæmias other than diabetes.

Gonorrhœal Conjunctivitis quickly cured.—LINDSAY REA, F.R.C.S.

Ten days ago this nurse, employed at the Lock Hospital, contracted acute blennorrhœa through an accident. The gonococcus was present in the discharge from each eye and both eyes discharged freely.

The nurse was at once isolated and not only was the eye bathed out with simple boracic lotion but the patient herself kept each conjunctival sac cleansed all the time. Unguentum atropinæ 1% with boracic acid (vaseline) was used and between the bathing and insertion of the ointment, the osmotic action of 10% magnesium sulphate was induced from five to ten minutes at a time, three and four

times daily. The magnesium sulphate was contained in Batten's hydrophthalmoscope—a patient quickly learns how to adjust the eye cup and at what height to hold the funnel.[1]

This morning there was neither gonococcus nor discharge present in either eye; the pupils were dilated as a result of atropine and the redness of the inflammation will be rapidly removed by use of a weak boric and zinc lotion. As the nurse was scrupulous in cleansing her eyes, she made a recovery which is a record for such cases.

Some time ago Mr. Wright described how he perforated the lid at the upper fornix and inserted a small rubber tube, but I do not agree with any operative procedure about the lids in cases of purulent discharge. Also, it is a rule in these cases of acute blenorrhœa of adults, never to use silver nitrate. I have seen a cornea slough away thirty-six hours after the application of 2% silver nitrate. Protargol drops, 10%, are quite safe and the lids should be painted with 15 to 20% protargol, but the important part of the treatment is the constant cleansing of the conjunctival sacs, and the recovery is greatly aided by the use of magnesium sulphate as described above.

Discussion.—Sir ARNOLD LAWSON said that long ago he arrived at the conclusion that it was immaterial whether one used magnesium sulphate or anything else for these cases; the merely antiseptic property of any lotion was of no importance. What was of importance was the frequent irrigation of the eye. He thought as good results would follow washing out the eye with saline as with magnesium sulphate.

This case reminded him of one he had had in which both corneæ were ulcerated and the eyes were streaming with pus on both sides. When he first saw the case it seemed hopeless. The patient was kept more or less constantly under morphia, and special nurses syringed out the eyes every half hour, at times every hour, with saline. There was no other treatment whatever. Within forty-eight hours the patient was practically out of danger, and when last heard of he was earning his living as a clerk in the City, both corneæ having soundly healed. Before he (Sir Arnold) had seen him, he had been treated with silver nitrate and mercury. He (the speaker) agreed that in suppurating cases strong drastic treatment did more harm than good.

In the main these bad cases must run their course, but if the discharge was not allowed to remain in contact with the cornea the condition would probably be healed.

Mr. M. S. MAYOU said that at St. Margaret's Hospital he had a large experience of gonorrhœal conjunctivitis; as there were some 250 cases a year, they varied in severity. He agreed with Sir Arnold Lawson that the important feature of the treatment in these cases was the constant washing and that the use of silver nitrate was not advisable, in the acute stage, though it was helpful in clearing up the terminal stages. Another measure of great service was, after bathing, filling the conjunctival sac with acriflavine, 1 in 1,500, and castor oil. The oily substance afforded a certain protection to the cornea, and kept the lid margins lubricated, so that the discharge could come out instead of being dammed up, and a non-irritating antiseptic was constantly present in the sac.

Right Epibulbar Growth.—CHARLES GOULDEN, F.R.C.S.

W. P., male, aged 76.

History.—Thirty years ago a growth was excised from the lower lip and there was at the same time an operation below the jaw, apparently for the removal of lymphatic glands. Two growths (? rodent ulcers) have been removed from the left cheek during the past five years.

Two years ago patient had a "stroke." He has noticed a swelling on the right eyeball during the past few months; this has gradually increased in size.

Right eye: Flat, fleshy, firm oval growth at 3 o'clock, outside the cornea for about 5 mm., and involving the cornea for about 2 mm. It is about 10 mm. in diameter in its vertical extent. The cornea has become opaque where the growth

[1] See LINDSAY REA: "Affections of the Eye in General Practice," 1930, p. 22, on which this instrument is illustrated and explained.

has invaded it. There are large prominent blood-vessels passing from the neighbourhood of the caruncle to the growth.

There is sclerosis of the lens nucleus. Right vision: $\frac{6}{18}$ with + 1·0 D. = $\frac{6}{12}$, illiterate.

Left eye: Nuclear sclerosis. Vision: $\frac{6}{24}$, illiterate.

Left Epibulbar Growth.—CHARLES GOULDEN, F.R.C.S.

U. M., male, aged 81.

History.—Indefinite. "The left eye has been sore for several months."

Right eye: Slight pterygium. Vision: $\frac{6}{24}$, with + 1·0 D. = $\frac{6}{9}$.

Left eye: An extensive fleshy growth surrounds the cornea for a depth of 12 to 14 mm. It has a marked raised edge which, below, is crenated. The cornea is extensively involved and completely vascularized. Vision: hand movements.

Discussion.—Mr. HUMPHREY NEAME said that the larger growth—that in the second of Mr. Goulden's cases—reminded him of an uncommon type of intra-ocular sarcoma of the choroid, which was very vascular. It seemed to correspond with one described in Collins and Mayou's "Pathology of the Eye,"—a perithelioma, in which the growth was grouped round vessels. These tumours might originate as endotheliomata and might not be really sarcomata in the ordinary sense. He advocated excision of this eye without delay. In the first case there was not the same urgency, but the growth in that case also was probably malignant.

Mr. G. G. PENMAN said that three months ago he had removed a growth closely resembling that in Mr. Goulden's first case. It had peeled off easily, leaving a clear cornea beneath, except just at the growing edge. The growth was examined microscopically and reported as having a very low grade of malignancy.

The patient still had the eye in his head; he was being seen periodically in view of a possible recurrence. The case was under the care of Mr. Doyne at St. Thomas's Hospital.

Mr. EUGENE WOLFF said that the larger growth was what the French called "the raspberry type of papilloma"; it grew in a characteristic way, spreading over the cornea like a pannus. In the section could be seen columns of cells, each containing one or two blood-vessels, which gradually grew over the cornea. Its character was usually regarded as between simple and malignant; it could easily be dissected off the cornea and sclera.

Mr. ARTHUR GRIFFITH said that the larger growth was like one which he himself had shown at a meeting of the Section in January, 1930, but which had been more shaggy on the surface. Examined microscopically, it had proved to be papilloma.[1]

Mr. TREACHER COLLINS said that he had had some experience of epibulbar growths of malignant character. A case of an epithelioma was sent to him with the idea of the eye being removed. Instead, he cut the growth off as close as possible to the cornea, and had radium applied afterwards for fifty minutes. He had followed up that case for several years had eventually ensued from a different disease. These growths on the surface of the cornea and there had been no return of the growth; a beautifully smooth scar had resulted. Death did not at first tend to dip down into the subjacent tissue, as did those beginning in the skin; the hard tissue of the cornea resisted downgrowth for a long time. The growths tended to spread over the surface of the cornea and backwards into Tenon's capsule. If the growth got into the sheath of a vessel it might extend down into the canal of Schlemm, and from that into the interior of the eye. He (the speaker) had read a paper on epibulbar growths before the Ophthalmological Society[2] showing the method of spread. That they did not at first go deeply was the reason why a surface removal followed by radium might result in saving the eye.

Mr. GOULDEN, in reply, said that in the case of the smaller growth the idea of conservatism was important, as the patient had a cataract in each eye, and the eye without the growth had the less vision. The eye with the small growth had $\frac{6}{12}$ vision, and hence it was important to see what conservative measures were possible, in spite of the patient

[1] *Proceedings*, 1930, xxiii, 618 (Sect. Ophth. 40); *ibid.* 841 (53).
[2] *Trans. Ophth. Soc. of the U.K.*, vol. xxxv, 215.

being 76 years old. Should the growth prove to be malignant, he assumed that the eye would have to be removed.

In the second case, if the growth proved to be malignant, something more serious must be done, as so much of the conjunctiva would have to be removed that there would be no covering to the interior of the orbit, so it would have to be exenterated. He would have a portion of the growth examined, to see what was its nature. He had regarded the growths in both cases as epitheliomata of the limbus, one more advanced than the other.

[*Postscript* 31.12.31.—A pathological examination shows that in each case the growth is an epithelioma.]

Some Points in the Fitting of Contact-Glasses.—A. RUGG-GUNN, M.B., F.R.C.S.

Looked at superficially, the technique of fitting contact-glasses seems fairly simple, and fortunately, in many cases it is so. There is, however, a considerable residuum of cases in which there is difficulty in acquiring tolerance and it is of certain of the reasons that give rise to this difficulty that I propose to speak. The manner of fitting which I employ and which I have described elsewhere I gradually evolved for myself. I am glad to say, however, that it is substantially the same as that used in the clinics of Professor Heine, of Kiel, and Professor Erggellet, of Jena. It is also practically identical with that employed at Budapest where there is a very active centre of contact-glass experimentation that is independent of Jena.

The determination of an exact scleral fit is of the first importance. In a short—and not entirely accurate—paper which I published last year, I stated that the best indication of this was a complete zone of scleral contact at the limbus—the important words being "at the limbus." This is true, but there are degrees of contact, varying from very slight to very considerable pressure. Further, the thickness of the limbal conjunctiva fluctuates considerably, especially in the presence of a contact-glass. Cocaine, of course, shrinks the conjunctiva and renders all observations in this respect valueless. Holocaine acts similarly but to a lesser degree. The final determination of the scleral curvature ultimately prescribed must be done without the aid of any anæsthetic. The ideal plan is to fit the contact glass provisionally selected in the morning and ask the patient to return in the afternoon, after he has worn it for an hour or two, before making the final decision.

The average radius of curvature of the adult sclera is about 12 mm. and the great majority of eyes in my experience, not excluding high myopes, take scleral brims ranging from 11·5 to 12·5 mm. radius. The smaller Zeiss set of trial glasses does not contain the 11·5 and the 12·5 series, but in my experience these are more useful than those of 11 and 13 mm. which it does contain.

The scleral brim of a contact-glass is a section of a sphere cut parallel to its equator and its mean diameter varies in size, according to whether it is cut nearer the equator or nearer the pole. Thus a section which fits perfectly one eye with a rather small cornea will, though quite correct with regard to its radius of curvature, say 11 mm., fail to fit a similar eye in which the corneal diameter is larger. This difficulty is not adequately met by applying a glass of slightly larger radius, though at present that is the only method of overcoming it in the case of Zeiss glasses. In Budapest they are now actually manufacturing contact glasses which have an intermediate zone between the corneal crown and the scleral brim. By some such method I have no doubt this serious difficulty will ultimately be met. At present, however, the uncertainty with regard to this measurement constitutes a very real obstacle towards attaining adequate comfort.

In the series of contact-glasses there are one or two in which the corneal crown and the scleral brim have the same radius, e.g. 11 mm. I shall refer later to the

effect these have on the cornea, but I would point out that this particular shape is also not conducive to a good scleral fit. With use they tend to settle down as it were and embrace the scleral conjunctiva too closely for comfort.

Of all eyes I think the high myope is the most difficult to fit. Whether it is the length of the eye which by increased leverage tends in movement to flick off the glass, whether it is merely its prominence, or whether laxity of the eyelids prevents adequate counter-pressure, the fact remains that very often the glass is difficult to retain. I think that for high myopes a wider scleral brim, giving a broader zone of contact, would be an improvement. At present contact-glasses of small corneal radius, i.e., those suitable for cases of high hypermetropia or aphakia, are provided with the widest brims. So much for the scleral brim.

Turning now to the corneal part of the contact-glass, it seems best, in considering its relation to comfort, to divide the corneal series into two groups: (1) those of small curvature which come into contact with the cornea only at the margin of the crown, i.e., in the position of the rim which separates the corneal crown from the scleral brim; (2) those of larger curvature which may come in contact with the cornea in the neighbourhood of its centre. It seems reasonable to infer that a glass from either of these groups will cause discomfort and possibly injury to the cornea. With regard to the latter I can say that I have never seen anything in the nature of an abrasion, but I have seen corneal œdema and cases in which patients have complained, after a few hours' wear, of dimness of vision and haloes around lights. The simplest method of studying these cases is to add a drop of fluorescin to the fluid meniscus. This brings out the relations of the contact-glass to the cornea in a way that is not equalled by any other method, e.g., slit-lamp observation. My small experience of cases of conical cornea—four patients altogether, two of whom were kindly referred to me by colleagues—suggest that observations with the aid of fluorescin are indispensable in this condition.

If I may be allowed to draw conclusions from the few observations I have made, I would say that contact near the limbus, as in the glasses of Group 1, is better tolerated than contact near the centre, that contact in the pupillary area of the cornea is very badly borne, and that contact in the intermediate zones of the cornea is least painful near the corneal periphery and becomes more painful the nearer it approaches the corneal centre. So far as comfort is concerned, Group 1 may be ignored. The glasses of this group are perfectly well tolerated.

The glasses of Group 2, however, are much more troublesome. Nos. 10 and 11 in the corneal series often touch the cornea, usually in what I take to be its most sensitive part, i.e., the summit of the cornea. This is obvious, when we recollect that the radius of curvature of the cornea (at the summit) varies from 7 to 8·5 mm. It is extremely rare to find a cornea the radius of which is not situated between these limits, except in cases of keratoconus. The average radius, that selected by Gullstrand for his schematic eye, is 7·7 mm. Where there is a difference of curvature between the scleral brim and the corneal crown, the former will take the weight, as it were, and prevent corneal contact. If, however, the two have the same curvature or very nearly the same curvature, the contact-glass slips over cornea and sclera and comes to rest on the summit of the former. The only way to prevent this is to prescribe a contact-glass of small corneal radius and direct that the residue of uncorrected error be neutralized by working a spherical addition on the outer surface of the contact-glass. For example, an eye myopic to the extent of 20 D and having a corneal radius of 6·7 mm. can be theoretically corrected by any one of the following five methods: (1) by a No. 11 contact-glass; (2) by No. 10·5 with the lens value of a − 2 D sphere worked on its outer surface; (3) by a No. 10 contact-glass + − 3·5 D sphere; (4) by a No. 9·5 + − 5 D sphere; and (5) by No. 9 + − 7 D sphere. The addition of − 7 D sphere to the contact-glass is apt to make the latter

rather heavy, but not impractically so. Such a wide range for selection, unfortunately, is seldom available, as it applies mainly to eyes of small corneal radius, and these are not notably frequent among high myopes. The principle, however, of choosing not the contact-glass which gives the best visual result but one approximating the curvature of the cornea itself and superimposing a spherical correction on its outer surface must be observed in the interests of comfort. It is possible also that a patient with a conical cornea would be content to wear a contact-glass which merely corrected his irregular astigmatism and wear over it ordinary spherical spectacles. The improvement in vision and absence of distortion in the resulting retinal image might be considered sufficient compensation for the inconvenience of this double method of correction.

I should like to make a point in connection with the method which I adopt, of measuring the distance between the vertex of the contact-glass *in situ* and the lack of any additional sphere that may be used to get full correction. The sphere is removed from the trial frame and a centrally perforated diaphragm substituted. Through the hole in the diaphragm the plunger of a small instrument like a depth gauge is inserted until it touches the vertex of the contact-glass. The distance is then read off in mm. The point I wish to make is that the diaphragm should be made of glass or, at any rate, should be transparent.

I would like also to say that, in my opinion, the practice that has arisen among certain dispensing opticians of undertaking the fitting of contact-glasses themselves is to be deplored. Many opticians now possess sets of trial contact-glasses, some of them very complete ones, which they lend or hire to ophthalmic surgeons who wish to use them. This is perfectly legitimate. At the present rate of exchange, a full set of Zeiss trial contact-glasses must cost somewhere about £260 and can hardly be considered an essential part of an ophthalmic surgeon's equipment. The actual fitting, however, should be in the hands of the surgeon and, indeed, it does not appear to me to be quite in keeping with the status of a dispenser.

With this remark, which I had much rather had been made by someone else, I bring to an end these somewhat disjointed notes.

The PRESIDENT said that in ordering a contact-glass combined with a spherical addition, it was, as Mr. Rugg-Gunn pointed out, necessary to give the distance between the contact-glass and the sphere in the trial frame. Having found the best contact-glass he (the President) advised a retinoscopy to save time and then to adding the required sphere, held in the hand, either touching or almost touching the contact-glass. This saved elaborate calculations when the sphere was 10 or 12 mm. away in a frame.

In conical cornea of extreme degree it was difficult to obtain a contact-glass which did not touch the thin centre of the cornea. Mr. Rugg-Gunn's advice to leave 6 or 8 dioptres of myopia to be corrected by ordinary spectacles relieved us of this difficulty.

The Use of Antiseptics in Ophthalmology.

By FREDERICK RIDLEY, F.R.C.S.

(From the Institute of Pathology and Research, St. Mary's Hospital, London.)

The following inquiry is concerned with the question whether antiseptic solutions instilled into the conjunctival sac are capable of destroying bacteria lying free in the tear fluid or on the surface of the conjunctiva. The conditions under which such an antiseptic has to act are well defined; it is subjected to a continuous dilution with tears, which are equivalent to a 10% solution of blood-serum in normal saline except for their lysozyme content. The efficacy of any antiseptic will therefere be determined by the following considerations :—

(1) Its ability to destroy the organisms present before it is rendered ineffective by dilution in tears.

(2) The length of time during which it will inhibit the growth of bacteria in spite of the progressive dilution.

(3) Its effect, if any, upon the natural protective agent lysozyme.

The rate of dilution in the normal conjunctival sac.—Using sodium fluoresceinate solution it was found that only 1 c.mm. could be introduced into the conjunctival sac without staining the lid edges and that a concentration of 1-200 could be employed without causing reflex epiphora. The subject was made to look down, the upper lid lifted and the minute drop delivered by a 1 c.mm. pipette placed on the conjunctiva above the cornea. The time at which no discoloration of the conjunctiva could be seen was noted, reflected daylight being employed. This was repeated using increasing dilutions until the dilution which gave no perceptible discoloration was reached.

Result.—Mean of Six Experiments.

Concentration of fluorescein	Time of disappearance of colour
1-200	660 secs.
1-400	360 ,,
1-800	168 ,,
1-1600	82 ,,
1-3200	30 ,,
1-6400 (invisible)	0

This experiment shows that a solution of fluorescein introduced into the normal conjunctival sac is diluted thirty-two times in 11 minutes. It may be seen also that the rate of dilution follows an arithmetical progression and not a geometrical progression as might be anticipated, that is a fixed weight of fluorescein is eliminated in a unit of time irrespective of the dilution. This is not the case with other substances such as argyrol and solutions of salts but is practically confined to dyes which are adsorbed on to the surface of the conjunctiva. In such cases an equilibrium is at once established between the adsorbed phase and the dissolved phase in the tear fluid. The mechanism of dilution in the case of the dyes is therefore comparable to the solution of a solid rather than to the dilution of a liquid. Its effect is to prolong the period during which the dyes are retained in the eye.

The following are the mean results of a series of experiments in which argyrol was used instead of fluorescein, cf. above.

Concentration of argyrol	Time of disappearance of colour
1-5	200 secs.
1-10	165 ,,
1-20	120 ,,
1-40	60 ,,
1-80	?
1-100 (invisible)	

In this case the argyrol introduced is diluted to 1-2 every 45 secs. approx. It follows that most of the solutions under consideration are diluted to at least 1-1000 of their initial strength in about eight minutes. It may be observed that the above figures suggest that the normal rate of flow of tears is approximately one c.mm. every 45 secs.

The bactericidal power of the antiseptics tested.—Since tears are similar in composition to a 10% solution of serum in normal saline this medium was used to test the bactericidal and inhibitory power of antiseptics in vitro. The antiseptics were put up in a series of dilutions having an interval of one half; the results are therefore approximate.

Result.

Antiseptic	Highest concentration tested	Concentration necessary to kill staphylococci or streptococci in 15 min. in 10 per cent. serum at 37·4° C.	Highest dilution at which growth is inhibited	Effect on lysozyme
Zinc sulph.	1%	> 1%	1-600	Nil
Mercury perchlor.	1-5000	1-400	1-25000	Nil
Mercury biniod.	1-5000	1-100	1-5000	Nil
Copper sulph.	1%	> 1%	1-100	Destroys
Silver nitrate (as chloride)	1%	1-1000	1-25000	Destroys
Coll. argentum	—	Nil	1-3	Nil
Acriflavine	1%	1-500	1-25000	Inhibits at 1-30000
Carbolic acid	1%	1-150	1-400	Nil
Argyrol	25%	> 25%	1-3200	Slight
Protargol	25%	> 25%	1-3200	Slight
Boric	2%	> 25%	1-5000	Nil
Merc. oxycyanide	1-100	1-200	1-5000	Slight
Eusol	1-1	1-2	Nil	Destroys
Mydriatics	—	Nil	—	Nil
Myotics	—	Nil	—	Nil
Cocaine	—	Nil	—	Nil
Mercurochrome	—	> 1%	1-3200	—

In considering the above data it is important to bear in mind that only staphylococci and hæmolytic streptococci were tested and it is unjustifiable to apply the results to other organisms without reservation. Thus, zinc sulphate is of undoubted value in angular conjunctivitis and it may be that other substances have a specific value. In view of the rapid dilution to which the antiseptics introduced are exposed it is clear that none can have any true bactericidal value except silver nitrate. Moreover, with the same exception, none can have any inhibitory effect on the growth of organisms in the conjunctival sac for more than a few minutes. It has been shown that the dyes are retained in the conjunctival sac for a relatively long period but this advantage is more than outweighed by the fact that the inhibitory action is delayed for several hours in the case of acriflavine.

Of the substances tested, silver nitrate alone may kill bacteria present in the tears and on the surface of the conjunctiva before it is rendered ineffective by dilution. It is usual to ascribe the beneficial action of silver nitrate to the desquamation which it produces and to say that it can have no antiseptic value since it is converted into the insoluble chloride by the action of the sodium chloride of the tears and tissues. This teaching is inaccurate. Silver chloride has the bactericidal and inhibitory action described above; not only is it effective in relatively high dilution, but, since it is precipitated in the superficial layers of the conjunctiva, it may be assumed to exert a powerful inhibitory effect until the superficial cells are removed. Silver nitrate destroys the lysozyme of the tears but at a dilution of 1-25000, which is actively inhibitory, it does not affect the lytic power of the tears as tested by the lysis of *M. lysodeicticus* technique. This substance therefore fulfils the three considerations laid down at the beginning of this inquiry. It is by far the most efficient of the substances examined and the results suggest that silver nitrate might be used with advantage in concentrations much weaker than those commonly employed. If this should prove to be the case, its use could be extended, since the discomfort at present associated with its application would be eliminated.

Section of Otology.

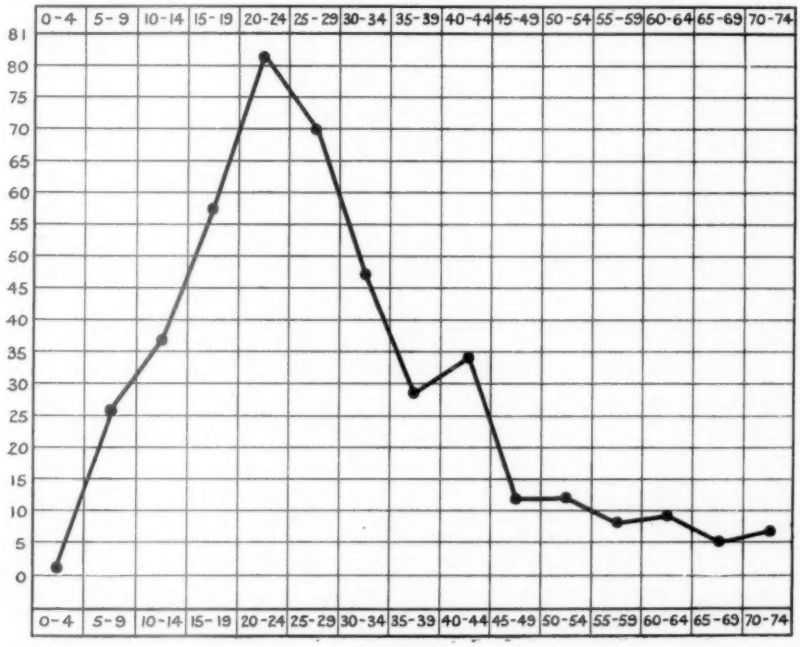
President—Mr. NORMAN PATTERSON, F.R.C.S.

[*November* 6, 1931].

Graphs illustrating Otosclerosis.

By DAN MCKENZIE, M.D.

THE four graphs here appended have been prepared from rather over 600 cases. For the purposes of a paper under preparation otosclerosis has been divided into three groups: primary, secondary, and a so-called incipient. The primary comprises cases in which no sign of otitis media exists; the secondary, cases consequent upon otitis media, catarrhal and suppurative; and the incipient, cases in which the deafness, though it may be of long standing and intractable to treatment, is slight.

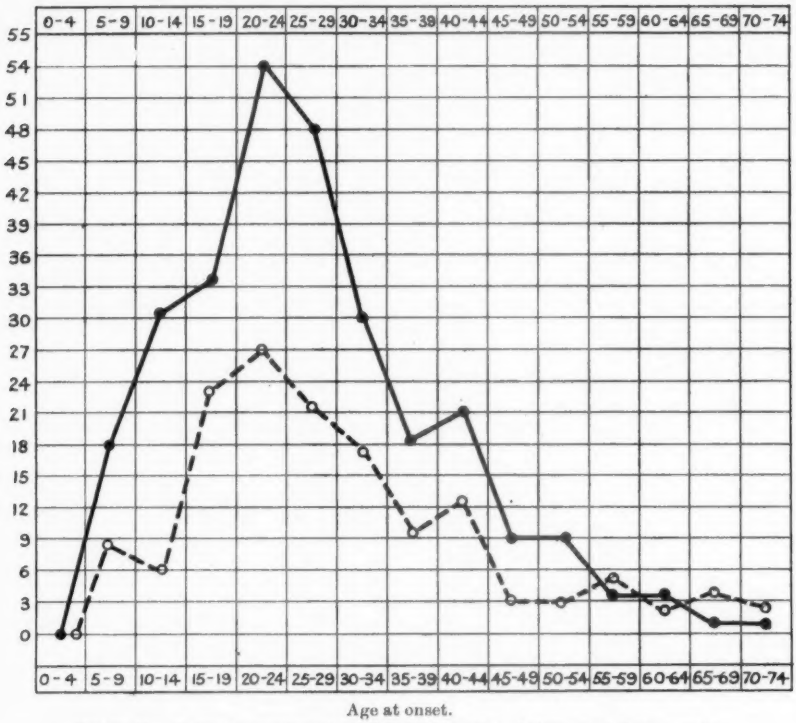


Age at onset.

CHART I.—Primary otosclerosis. Both sexes. Corrected for population. 426 cases.

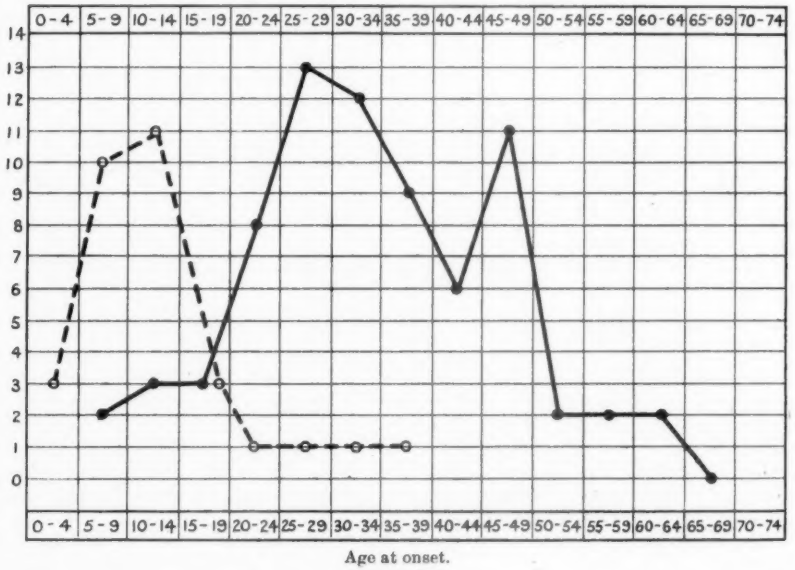
The graph in fig. 1 shows the number of cases at the different quinquennial age-periods, brought into ratio with the general population. It will be seen that the highest peak of frequency occurs between 20 and 24, and that the bulk (80% in fact) of cases begins in the first half of life, namely, before the age of 35. After that year, the figures decline, the tracing showing a slight rise in the 40-44 age-period. It shows, also, that no age is exempt. I have records of otosclerosis starting as early as the age of 3, and as late as the age of 70.

The graph in fig. 2 was prepared to show the ages of onset of the two sexes separately. The preponderance of females (two out of three) raises the question



Age at onset.

CHART II.—Primary otosclerosis. Male and female. Interrupted line = male.

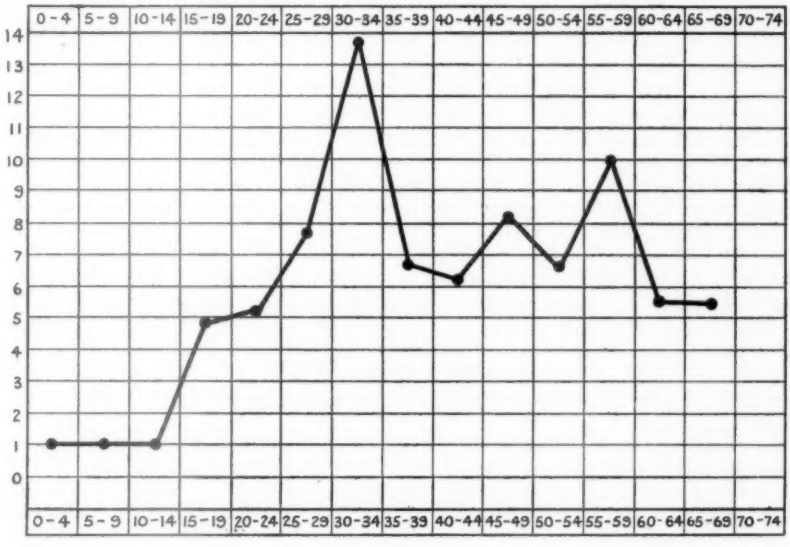


Age at onset.

CHART III.

whether some peculiarly female influence is operating, whether, that is to say, any connection with the female sexual life can be demonstrated. But the tracings for both sexes (continuous line, females; interrupted, males) run nearly parallel, even to the slight rise between 40 and 44. Towards the end of life the male line rises higher than the female, but the numbers at this period are few. Thus the incidence of otosclerosis, relative to age, is the same or nearly the same in both sexes, when allowance is made for the excess of women, and so there is no hint as to the reason for this excess in the age-incidence of the disease.

In fig. 3, the ages of onset in secondary otosclerosis are plotted out, the suppurative being the interrupted, and the catarrhal the continuous line. The graph shows how the former begins in most cases before the age of fifteen, while the catarrhal peak of high frequency is not reached until the 25-29 age-period, five years later than that in primary otosclerosis. It will be noticed that a late rise in



Age at onset.

CHART IV.—Otosclerosis incipient. Corrected for population.

frequency is present here as well as on the primary graph, but that it also in the catarrhal group occurs five years later.

The difference seems to show that the discrimination in the records between primary and catarrhal otosclerosis has been correctly made.

The final graph, that for the so-called incipient otosclerosis, we find to be different from all the others. The highest peak is not reached until the 30-34 age-period, that is to say, it occurs ten years later than in primary, and five years later than in catarrhal otosclerosis. Further, this form begins more frequently in the last half of life than in the first half. The reasons for the difference I cannot surmise.

CASES.

Tumour of (?) Meninges causing Ear Symptoms and Involvement of Certain Cranial Nerves.—NORMAN PATTERSON, F.R.C.S. (President).

Male, aged 56. Deafness and tinnitus in right ear since 1918—after influenza. Noise always continuous, never beating. Bleeding from right ear January 23, 1931, followed a slight sneeze; blood poured from the ear for about four minutes; afterwards repeated small hæmorrhages. Granulation tissue was noticed in the meatus. April, 1931, severe hæmorrhage from right ear, lasting one hour and twenty minutes, stopped by gauze plug soaked in adrenalin. Wasting of right side of tongue observed. Blood-pressure, 160/125. Slight recurring hæmorrhage; on August 5, 1931, severe hæmorrhage. Admitted to hospital August 6 and kept in for eight weeks. During my absence my colleague, Mr. Morris, intended to operate but instead he removed a fragment of "polypus" for section. X-ray treatment was instituted on September 18. No more bleeding since then. Before that there had been a little bleeding almost every day, preceded by slight headache. The headaches recently have been continuous—they are located in the occipital region. With Bárány box in the left ear he can hear loud spoken words at about 6-9 inches. He feels that he would spin round if he did not hold his head straight. Dizziness has been severe during the last five weeks. Voice has been husky since April, 1931. During the last two or three months patient has had to wash solid food down with water.

On examination.—There are a few small venules over the right mastoid process and there is an artery pulsating over this process. There is very slight weakness of the upper and lower face. According to one observer there is wasting of the right side of the soft palate and right sterno-mastoid. Another observer states that there is slight deviation of the palate to the left on phonation, and possibly slight weakness and wasting of the right sterno-mastoid. The tongue is much wasted on the right side and deviates strongly to the right. Skiagrams show apparent increase in vascularity and density of the right temporal bone, and the right parietal bone immediately above it. The sella turcica is slightly enlarged with slight erosion of the clinoid processes. In one skiagram the right external auditory canal has a rather irregular outline.

Mr. Hugh Cairns, to whom I am greatly indebted for his thorough investigation of this case, thinks that the patient is suffering from a tumour of the right cerebello-pontine angle affecting the twelfth and, to a less extent the eleventh to the seventh nerves inclusive. He considers that the histological appearance suggests a hæmangio-blastoma or possibly an angioblastic meningioma. The pathological department of the hospital label the tumour "hæmangio-endothelioma."

Plexiform Angeioma.—M. VLASTO, F.R.C.S.

Mrs. H., aged 63, came to the West London Hospital complaining of unbearable tinnitus on the left side. She had first noticed the tinnitus six months previously. The noise is pulsatile, and is worse when the head is in the dependent position.

There is a network of enlarged vessels behind the left ear, and a soft thrill is easily distinguishable with the fingers. With the stethoscope one can hear a loud murmur over a relatively wide area. There is little doubt that the diagnosis is a plexiform angeioma. The case is shown partly because tinnitus from this cause is uncommon and particularly because suggestions as to treatment are requested. Dr. Isabelle Horsley, who sent the patient to see me, is insistent that some treatment must be carried out, on account of suicidal tendencies.

Blood-pressure 160/90.

Discussion.—Mr. SOMERVILLE HASTINGS said the extraordinary feature of this case was that the symptoms had only been noted for six months, though one thought of this as a congenital condition, or one which was early evident.

If pressure was made on the common carotid, the bruit ceased; so that apparently the tumour was fed mainly by the common carotid and its tributaries. If the tinnitus disturbed the patient, as the history indicated, it would be worth while to tie the common carotid, though the procedure might not be a success, as an anastomotic circulation might be established and the symptoms return.

Mr. ALEXANDER SHARP said he had been interested in the patient's statement that during the last three weeks the symptoms were much relieved after the feeling of a bang in the head on two occasions. Was the explanation of the bang that the obstruction to the blood-flow suddenly gave way?

Mr. HERBERT TILLEY said that the symptom of hearing "a bang in the ear" interested him because on rare occasions and when falling off to sleep, he had experienced it, and it was very disturbing. In Gowers' textbook the author ascribed the symptom to a sudden contraction of the stapedius muscle.

THE PRESIDENT said that six years ago a medical colleague sent him a somewhat similar case, in an old gentleman. The external carotid was tied, and the symptoms disappeared at once, and had not returned.

Mr. VLASTO in reply said that he had no explanation to offer as to why the tinnitus had come on so suddenly six weeks ago. Until it had been demonstrated to him in the adjoining room, he had been under the impression that compression of the carotid did not stop the pulsation. He now agreed that it did; at the same time, he would add that the murmur and thrill were less marked at the present time than at any time during which the patient had been under his observation. If consent were obtained, he would ligate the external carotid as suggested, and show the case at a later meeting. Skiagrams of the skull showed that the cranial sutures were abnormally evident, and Dr. Worth had suggested that there was evidence of increased intracranial tension. There appeared to be a possibility—as Dr. Parkes Weber and others had pointed out—of an associated vascular tumour of the meninges, in which case a perfect result from the operation might not be achieved.

Postscript.—January 8, 1932. The external carotid was ligated on the affected side and the tinnitus has completely ceased. The patient still complains of an intermittent thumping in the head. She is, however, glad that the operation was performed.—M. V.

Fractured Base of Skull, with Severe Complications. Recovery.—WILLIAM IBBOTSON, F.R.C.S.Ed.

Woman, aged 25. First seen 16.8.30.

History. 16.8.30.—Motor accident, resulting in fracture of base of skull; hæmorrhage from both ears; conscious, but severely concussed.

19.8.30.—Paresis of right seventh cranial nerve, with fibrillary twitchings under right eye; no other cranial nerves affected.

20.8.30.—Complete right-sided facial paralysis.

25.8.30.—Patient had a fit, initiated with a right-sided aura and affecting the right side of the body.

30.8.30.—Severe headache on right side; definite evidence of acute mastoiditis (right), there having been suppuration from the tympanic cavity for several days. A slight serous discharge still persists from the left ear.

Operation.—Conservative mastoid drainage, right; much free pus and altered stale blood being evacuated, thus revealing a fine, tortuous fracture, extending vertically upwards through the squamous bone. As more bone was removed superiorly, hæmorrhage became much more profuse and pulsating, so that it was soon obvious that some important artery was bleeding. Subtemporal decompression was then performed, when the middle meningeal artery was found to be ruptured in its passage in the groove on the great wing of the sphenoid. Ligature being quite impracticable, I decided to apply cut muscle to the bleeding-point, and this was done with a portion of mobilized temporalis. The effect was very rapid, for the bleeding soon ceased, nor did it ever recur.

Progress.—There was persistent and troublesome suppuration, both beneath the scalp flaps and in the mastoid region, but eventually this ceased and to-day the condition is as follows:—

Wounds healed; no signs of facial paralysis; hears a whisper with right ear at 25 ft.; general health excellent; is back at work.

Specimen of a Temporal Bone, with Congenital Absence of the External Auditory Meatus.—E. D. D. DAVIS, F.R.C.S.

The specimen was obtained from a woman, aged 56, who died from a fractured skull.

The auricle was rudimentary and deformed, with no sign of an auditory meatus. The temporal bone was dissected and, with a fret-saw, thin layers of dense cancellous bone were shaved off until the middle ear and mastoid antrum were exposed. There was no indication of even the position of the meatus, and both the middle ear and mastoid antrum were covered by a considerable thickness of cancellous bone. There was no drum and no malleus, but the inner wall of the middle ear, Eustachian tube and canal for the tensor tympani are normal in appearance. The incus and stapes, which can be seen, are deformed. The mastoid antrum, internal auditory meatus, and auditory and facial nerves are normal.

There is an abnormally deep Meckel's cave for the Gasserian ganglion.

Recovery after Meningitis with Hæmolytic Streptococci in the Cerebrospinal Fluid under Direct Observation.—T. B. LAYTON, D.S.O., M.S.

John F. N., aged 25. Had had ear discharge for twenty years when, on 24.2.31, he noticed that something had come out of the ear. He was treated at his own home for twelve days, during which period headache was at times so severe that he did not sleep for four nights.

On 9.3.31 he was admitted to hospital and a polypus was removed under general anæsthesia. Twenty-four hours later he was transferred to the South-Eastern Fever Hospital as a case of cerebrospinal meningitis.

Admitted at 10 p.m. The diagnosis was accepted provisionally by the admitting medical officer, who performed a lumbar puncture, drew off 60 c.c. of turbid fluid under high pressure and injected 40 c.c. of anti-meningococcal serum. When seen by me next morning, there was profuse left ear discharge and the patient was in an advanced stage of meningitis with rigid neck and back and Kernig's sign. A further lumbar puncture was performed that morning (11.3.31) and 35 c.c. of fluid were withdrawn, 25 c.c. anti-meningococcal serum were injected into the theca, a further 25 c.c. being given intravenously. The report from the laboratory on this fluid stated that numerous Gram-positive diplococci and short-chained streptococci were seen in the fluid on direct examination—a subsequent report stated that there was a pure growth of hæmolytic streptococci with abundant colonies.

The mastoid was opened at 5 p.m., i.e., forty-eight hours after the removal of the polypus. A dense bone was found. From the roof of the middle-ear a track of disease could be traced to the floor of the middle fossa, but no definite change could be recognized on the dura mater. The pinna was tied and sewn forward and the cavity hosed with a gallon of saline.

This hosing was repeated thrice daily for three days and then continued with decreasing frequency till the end of the week, when he was out of danger.

12.3.31, (a.m.)—Lumbar puncture, 25 c.c. 10 p.m., lumbar puncture: only one or two drops of fluid.

14.3.31.—Lumbar puncture, 25 c.c., fluid not so turbid. 40 c.c. anti-streptococcal serum intravenously.

16.3.31.—Lumbar puncture, 15 c.c., fluid almost clear.

The wound and drumhead are now healed.

Acute Mastoiditis and Meningitis with Streptococci observed on Direct Examination of the Cerebrospinal Fluid.—R. J. CANN, M.S.

J. B., a girl aged 19, admitted to Guy's Hospital with signs of acute mastoiditis and meningitis.

Mastoidectomy performed; pus and granulations found in antrum and cells. Dura mater of both fossæ was exposed and appeared normal. Lumbar puncture produced turbid fluid in which streptococci were demonstrated on direct examination and by subsequent culture. Recovery after repeated daily lumbar punctures.

An Unusual Case of Zygomatic Mastoiditis.—W. A. MILL, M.S.

Frank F., aged 7, first seen April 30, 1931. Had had earache for four days and a blood-stained discharge for one day. Temperature, 101° F.; marked tenderness over mastoid. Small swelling in parotid region, just in front of tragus. Appearance suggested adenitis of pre-auricular glands, but no cause could be found for this. The swelling was well below the zygomatic arch and the latter was not tender. Nor was there any swelling in the temporal fossa. Marked trismus was present.

The same evening, at operation, extensive disease was found in the mastoid. The lateral sinus and dura of the middle fossa were exposed. Cells were found in the root of the zygoma and it was thought that healthy bone had been reached in this direction.

Following operation, the pre-auricular swelling continued to increase, and finally fluctuation was detected. The swelling was limited above by the zygomatic arch and suggested at first sight the swelling of mumps.

On May 7 the abscess was opened and a tube inserted. When a finger was introduced into the wound it was found that the deep surface of the zygoma was bare. It was decided not to remove it but to await developments.

The patient's condition improved greatly but trismus continued to be marked. On May 16 another anæsthetic was given; the zygoma was found to be completely bare of soft tissues and its surface was roughened. The arch was removed up to and including part of the malar bone.

The original mastoid incision was prolonged upward and forward, and a search was made through the posterior wound for cells in the zygomatic region. A few small cells were found just above the temporo-mandibular joint.

Healing proceeded steadily except that an enlarged cervical gland suppurated and required incision. The tympanic membrane is now intact.

The case is shown because the limitation of the swelling to the parotid region is regarded as unusual.

Keloid of Mastoid Scar.—E. BROUGHTON BARNES, F.R.C.S.Ed.

Patient, male, aged 24.

History.—Acute mastoid operation seven years ago; widely pneumatized mastoid. The middle ear is completely healed. There is an apparently quite normal membrane and the hearing is perfect. There is a large keloid over the mastoid.

[*December* 4, 1931.]

Cholesteatoma in Aural Suppuration: Its Relation to Prognosis.

By T. B. Jobson, M.D.

At our meeting in November, 1930, Dr. Dan McKenzie read a paper on the "Pathogeny of Aural Cholesteatoma," in which he advanced the theory that aural cholesteatoma is a primary condition, an altered state of the epithelium lining the middle ear, an epidermoid growth, and that the suppuration, so frequently found associated with it, is secondary. This idea is contrary to textbook teaching. It required an iconoclast like Dr. McKenzie to disturb a preconceived notion and rouse us out of our lethargy. The idea is not entirely new, but has hardly received the attention it deserves. We owe a debt to Dr. McKenzie for his work on this subject.

To-day I wish to bring further evidence in support of the hypothesis that cholesteatoma is a primary condition which greatly increases the gravity of cases of aural suppuration.

In treating suppurative otitis media by zinc ionization, one is struck by the difference in the behaviour in ears with cholesteatoma and those without. In 1923 I published some results of treatment by ionization. None of the cases diagnosed as cholesteatoma were cured. But omitting these cases, the percentage cure was 80%. I will quote my remarks on these cases:—

"*Attic and Cholesteatoma Cases.*

"These were of the well-known type with tiny attic perforation either in Shrapnell's membrane or burrowing under the anterior or posterior ligament of the malleus. The membrane itself was glued to the inner wall of the tympanum by cholesteatoma, and was by the pneumatic speculum shown to be either totally fixed or mobile only in small areas. These cases, which generally have only a scanty foul-smelling discharge, usually have symptoms of toxæmia, such as headaches, giddiness, and chronic ill-health. They are the most dangerous class, always on the brink of a calamity. In the hope of benefiting this type of case I tried various preliminary methods of treatment, such as drops of liquor pepticus, liquor pancreaticus, and aniline oil with spirit. After these had been used for a week, I washed out the tympanum with warm ether, followed by the zinc solution, and then ionized. My hope was that the cholesteatoma would be partially disintegrated and thus capable of being washed out. Not one of these cases was cured. I am firmly convinced that such cases are not curable by any form of antiseptic treatment nor by ionization.

"Cholesteatoma is in a class by itself. Our knowledge of its causation is incomplete. At present the only efficient treatment is a radical mastoid or possibly ossiculectomy operation. Occasionally a case that seems to be cholesteatoma does dry up, leaving a wax-like fixed drum, but such cases are the exception."

My ideas to-day are nearly the same, but with the flood-lighting cast on the subject by the theory that cholesteatoma is the primary condition with suppuration grafted on it, these statements seem more illuminating.

The results of other surgeons who use ionization in the treatment of otorrhœa show how resistant to treatment is the group known as "attic" cases. In some of the published results, the percentage cure is nil—in others very small.

Now why should these "attic" cases differ so markedly from ordinary cases of tympanic sepsis? Why should "attic cases" be so resistant to conservative treatment? I suggest that the reason is the evil combination of cholesteatoma with sepsis, so that "attic sepsis" becomes almost equivalent to "requiring a radical mastoid operation" when entered on the case sheet. The cholesteatoma renders the

sepsis in the attic inaccessible. The layers of shed epithelium make a suitable nidus for organisms. The folds of skin protect the organisms from any antiseptic action that can be brought to bear on them. The blood supply of the cholesteatomatous wall is poor. The secretion of antiseptic mucus, which plays such a part in the fight in ordinary tympanic sepsis, is greatly lessened. The perforation is usually very small, affording very poor drainage and aeration.

All these factors are familiar to you. I recall them now because I want to look at the attic problem on the hypothesis that cholesteatoma is a primary condition. Why should there be an attic problem at all? Why is it that the attic is always singled out as the lair of this malevolent couple, cholesteatoma-sepsis? I suggest that it is a natural sequel of the anatomical shape of the middle ear. If we conceive a slow hyperplastic process involving the mucosa of the middle ear, we should expect the narrow clefts of this space to be obliterated first. We have a cavity roughly wedge-shaped. The distance between the true tympanic membrane and the inner wall is but a few millimetres. This distance increases to 6 to 8 mm. in the epitympanic space. I suggest that a hyperplastic process starting from the periphery slowly fills in this lower tympanic space. By this process the lower portion of the tympanum is shut off before sepsis arises. The attic is then the only space left where sepsis can occur. In attic suppuration, one invariably finds the membrane adherent to the inner wall to a greater or less extent. Frequently it is completely adherent. When partly adherent, it may give the false impression of a large perforation and frequently gives rise to a wrong diagnosis.

Case 1 shows this process in a very early stage. As a rule these cases do not come under observation until late. If our hypothesis is correct, the cholesteatomatous hyperplasia would precede the sepsis by a considerable period. The latter might be long delayed or never superadded. One can well imagine the process reaching the stage when it had fixed the membrane and partially filled the epitympanum without any sepsis occurring. The case would be regarded as one of chronic adhesive deafness. Indeed the thought arises: "Are some of our cases labelled 'chronic adhesive deafness' those in which there has been a mild degree of this cholesteatomatous hyperplasia, where the process has not progressed and where no secondary sepsis has supervened?"

If we postulate cholesteatoma as primary, we do not necessarily unite it with sepsis at all. Their union is pregnant with danger. The longer they can be kept apart the better. Their divorce defies the courts of otology.

How does the introduction of sepsis take place? Does the cholesteatoma cause a perforation of Shrapnell's membrane through which sepsis reaches the attic? Or does the septic invasion take place through the Eustachian tube? Can it occur in both ways?

Diagnosis.—When the case has reached the stage in which obvious cholesteatoma is present, the diagnosis presents no difficulty. The earlier the case is seen the more difficult is the diagnosis. In a moderately advanced case one relies on:—

(1) The history: generally a painless slow onset. Frequently the patient cannot give a date of onset. He is probably more concerned about the fœtid odour from his ear which only occurs after septic infection, than anything else.

(2) The tympanic picture: the tiny perforation in Shrapnell's membrane, or a burrow leading up under the anterior or posterior ligament of the malleus.

(3) The partial or complete fixation of the membrane when tested with Siegle's speculum.

(4) The character of the discharge: generally scanty, often thin, but invariably with characteristic fœtor, associated with cholesteatoma when combined with sepsis.

(5) Bacteriological examination of the discharge shows a mixed septic infection with squamous cells and possibly cholesterin crystals. The discharge may be so slight that it

is not noticed by the patient. It may be intermittent and sometimes absent for many months.

(6) Symptoms of toxæmia may or may not be present. It is common to find headache, lassitude, inability to think clearly, early fatigue, sallow colour. On the other hand, one may meet an advanced case without any of these symptoms.

It is in the earliest stage that the diagnosis is so difficult. If our hypothesis is true, our object should be to diagnose these cases before sepsis has been introduced and to do our best to prevent it. Cases of slight deafness, when the membrane is partially adherent, and when there is a blush over Shrapnell's membrane, should be watched very closely, as possibly being cholesteatomatous, and any sepsis in the nose or throat dealt with.

It sometimes requires very careful examination to appreciate accurately the geography of the membrane in cases which have reached the stage of suppuration. The patient may complain of a bad-smelling discharge. The examination may confirm this statement—a little pus is visible. When this is wiped off with a cotton wool probe, it is found to have the characteristic fœtor. The membrane now shows up clearly. It may present no sign of a perforation. On applying suction no pus may be obtained, although the membrane may look thickened and retracted and lack mobility. Several examinations may be necessary before the tiny track is located.

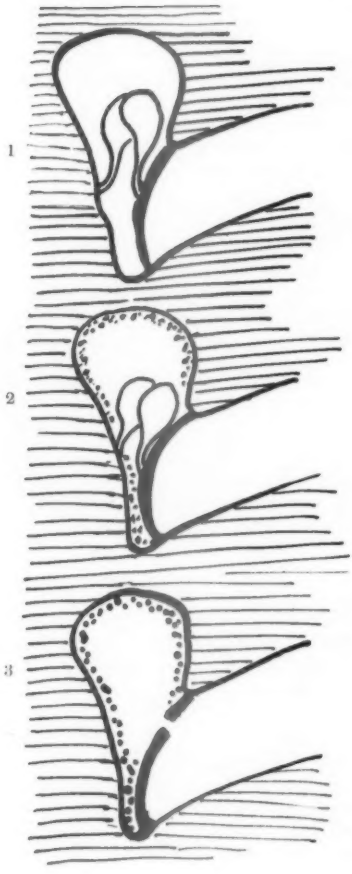
The bone-absorbing faculty of cholesteatoma is most remarkable. The insidious manner in which wide areas of bone are dissolved without warning is characteristic, whilst the sudden extension of the process to some vital spot is dramatic. The first sign the patient may have is that his face is paralysed. Or maybe the disease has eroded a canal and a sudden labyrinthine storm is the first danger signal. Enormous areas of dura may be laid bare with hardly a symptom.

Herein then is the danger of cholesteatoma. It is an insidious, relentless enemy. As soon as the diagnosis of cholesteatoma is made, the patient must be warned of its possibilities and dangers. The surgeon, however, cannot guarantee cure by either conservative or operative treatment.

Take the case of a patient who comes to consult you for an occasional slight discharge from the ear without an ache or a pain and with quite good hearing. It will require some tactful reasoning to convince such a man that he has a dangerous complaint; that he is living on the edge of a volcano which may explode at any moment. To him one ear discharge is like any other. His discharge is perhaps much less than that of some of his friends, although he will admit that the "smell" is unpleasant. Again, hearing may still be fairly good in that ear and his livelihood may depend on his hearing. If both his ears are affected the problem becomes very acute. His life is not safe while the cholesteatoma is there. Yet the surgeon cannot guarantee him a good hearing ear or a dry ear. But he can offer him the probability of a dry ear and the possibility of fair hearing, with an assurance of almost total elimination of complications which may threaten his life. It is for the patient to decide. Patients with toxic symptoms such as headache and giddiness as a rule require little persuasion. They realize their danger.

Prognosis.—The presence of cholesteatoma in the middle ear, combined with sepsis, makes the prognosis infinitely worse. Tympanic sepsis without cholesteatoma is usually curable before the question of operation arises. I speak of course of chronic suppurative otitis media. I venture to think that the large majority of chronic cases which come to mastoid operation are cases of cholesteatoma plus sepsis. On examining statistics of radical mastoid operations when the presence or absence of cholesteatoma has been noted, one finds that they show a high proportion of cholesteatoma.

Although these cases of cholesteatoma usually progress slowly and insidiously one occasionally meets an exception that proves the rule. Case 4, although an



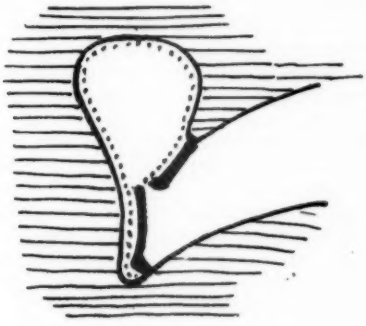


DIAGRAM 4.

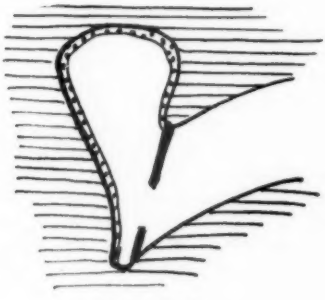


DIAGRAM 5.

THE ATTIC PERFORATION.

Diagrams showing how the attic may become shut off from the lower tympanic cavity by hyperplastic otitis. The membrane becomes adherent to the inner wall. The upper half of the membrane becomes the virtual floor of the attic. If suppuration supervenes the perforation occurs somewhere in this floor.

1. Normal.
2. Lower half of membrane adherent to inner wall.
3. Perforation above short process of malleus. This is seen in sketches of tympanic membranes of Cases 1, 2, 4 and 6.

DIAGRAM 4.—Illustrating the perforation under the anterior or posterior fold of the malleus. This is usually a tiny track leading to the attic and often difficult to observe. It is seen in the sketches of tympanic membranes of Cases 3 and 7.

DIAGRAM 5.—Showing the conditions present in an ordinary case of tympanic sepsis (non-cholesteatomatous). The perforation is in the lower half of the membrane which stands out clear of the inner wall. Although the attic is involved by the sepsis, there is fair drainage. The attic is accessible for treatment by antiseptic drops or ionization.

undoubted case of "attic" suppuration, has shown some improvement as the result of treatment. Occasionally one sees a case in which the condition appears to dry up, leaving a deformed wax-like membrane. Now and then this may occur in the presence of a low-grade infection. But, granting all this, one must admit that attic cholesteatoma is a dangerous condition, slowly progressive, and usually requiring a radical mastoid operation to insure the patient against a sudden disaster.

If we adopt the hypothesis that cholesteatoma is primary—that it is due to some defect in the epithelium of the middle ear—we have to keep clearly before our minds that we have two conditions to treat, the cholesteatoma and the suppuration associated with it. We have to deal with a cavity full of moist epithelial débris and pus, approachable only through a pinhole opening. Contrasting this with the condition present in acute suppurative otitis media, we have some resemblance in that we have a middle ear full of pus and a pinhole perforation. In the latter case, however, we have a mucosa capable of complete resolution. In the former we have an altered mucosa incapable of becoming normal. Even if we cure the suppuration, the condition of cholesteatoma remains and the suppuration may recur.

To obtain an improvement or cure in the condition of cholesteatoma we must establish free drainage and aeration. Usually a radical mastoid operation is necessary. Free drainage of the attic is essential. Even then we cannot be sure that the mucosa will give up its cholesteatomous tendency. After a perfectly executed radical operation the mucosa may still persist in shedding epithelium and the characteristic fœtor may be noticeable. Indeed, a radical mastoid cavity obtained by operation on a case of cholesteatoma is never free from the danger of relapse. Such a cavity requires periodic inspection by an aurist. Its behaviour sheds a good deal of light on the nature of cholesteatoma.

How often one finds that mastoid cavities, although resulting from operation by first-class surgeons, refuse to become dry. For years, even for ever, a little fœtid secretion continues to come away. Little areas of crust formation occur. Removal of these shows an area of whitish thickened epithelium. The behaviour of these cavities is really rather extraordinary. They sometimes dry up and remain dry for long periods. And yet they may relapse into their old bad habits of crust formation, which may conceal pus and possibly granulations. Energetic treatment may result in a clean cavity, but there is always the tendency to relapse. The epithelium has that characteristic tendency to proliferate. This I take to be the original epidermoid tendency transmitted from the epithelium of the middle ear to that of the mastoid cavity. In cases that have been grafted I have seen this condition, although *a priori* one would expect the tendency to be lessened in a grafted case—or at least to find the actual grafted part of the cavity free from this degeneracy.

When one dwells on these cases one wonders over and over again why they should behave in this remarkable manner. If cholesteatoma is a primary condition, is it a congenital one? If congenital, can it be prevented? Ulrich states that cholesteatoma of the middle ear is never associated with a central perforation. Ulrich of Basle states that out of 458 operations 98% had epitympanic perforations. Why should this be so? Is the explanation I have advanced the true one? Nager draws a parallel between cholesteatoma and tuberculosis. Not a convincing parallel to my mind, but worthy of notice. Certain diseases show an increased cholesterin content in the blood; the amount varies.

Unfortunately, cholesteatoma of aural origin does not betray itself by yielding an increased cholesterolæmia. We are deprived of this aid to diagnosis. But is it possible that some treatment might be devised that would alter the cholesterin formation of the blood and so alter the behaviour of the cholesteatoma?

ILLUSTRATIVE CASES.

Case 1.– Miss E. T., aged 45. Patient seen in March, 1931. Only complaint was slight deafness in left ear. No history of pain or discharge.

Examination showed a tiny perforation above the short process of the malleus, a minute sentinel granulation below the perforation, with a streak of pus over the margin of the malleus. Typical fœtor of cholesteatoma. Membrane fixed to inner wall in anterior half, mobile posteriorly.

This appeared to be a case of attic cholesteatoma found at a very early stage. There was no history of previous ear trouble of any kind. Her sister has advanced otosclerosis. Hence

FIG. 1a.

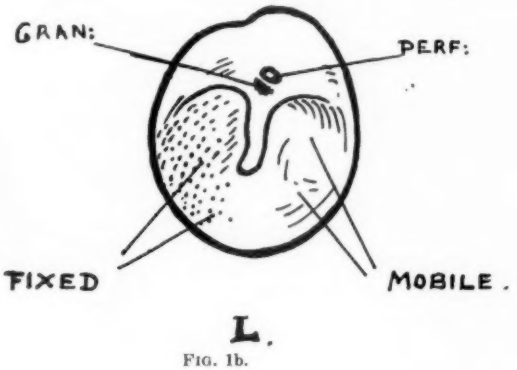


FIG. 1b.

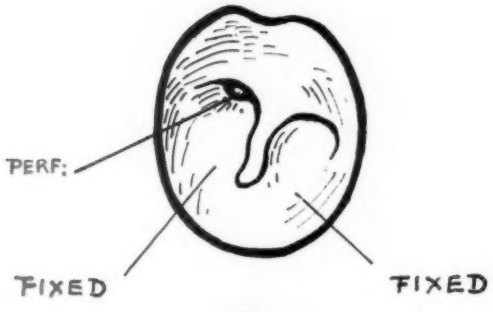


FIG. 2.

FIG. 1a.—*Case* 1. E. T., left membrane. Shows typical site of attic perforation just above short process of malleus. It corresponds to the thin area described by Gruber.

FIG. 1b.—*Case* 1. E. T. Left.

FIG. 2.—*Case* 2. P. S. Right.

this patient's anxiety to have early advice regarding her deafness. This patient has been under observation for six months. Symptoms are very slight. The perforation scabs over from time to time. It will be interesting to see if this case develops into a classical example of attic cholesteatoma.

Case 2.—P. S., a girl aged 6½, seen in 1927.

History of otorrhœa for two years following scarlet fever. Membrane showed a tiny track under post-ligament of malleus. Thin pus sucked out. Typical cholesteatoma fœtor. Membranes fixed below.

Conservative mastoid operation performed. Intermittent discharge continued.

Admitted to hospital May, 1931. Radical mastoid operation. Nests of cholesteatoma in mastoid process and tympanum.

This case shows a typical site for perforation, viz., in what is virtually the floor of the attic.

Treatment by antiseptic drops and ionization made no improvement.

Case 3.—F. L., a man aged 26, seen January, 1928. Deaf in left ear since childhood. The ear used to discharge, but had been dry for years. A month previously he noticed a weakness of left side of face and could not shut his eye. He had complete facial paralysis on

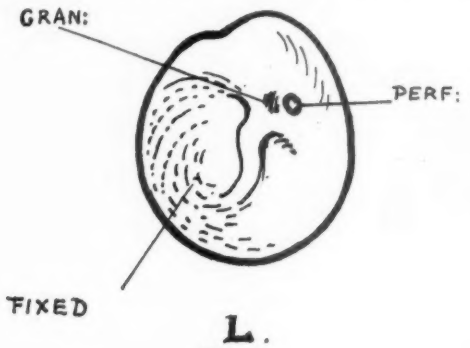


FIG. 3.

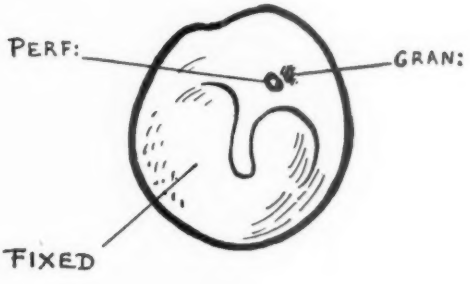


FIG. 4.

FIG. 3.—*Case* 3. F. L. Left.
FIG. 4.—*Case* 4. W. K. Left.

the left side, yet made no complaint about his ear, and he did not realize that he was seriously ill.

At the radical mastoid operation large sequestra were removed from the labyrinth. The dura above the tegmen was exposed by disease for over an inch. The mastoid cavity dried for a time, but has subsequently given great trouble by formation of crusts and granulations with the typical fetor. This case illustrates the slow, almost symptomless, but relentless spread of cholesteatoma, actually causing a large sequestrum in the temporal bone with destruction of the facial nerve without any warning.

Case 4.—W. K., a man aged 28, seen in 1923 on account of a continuous banging noise in the left ear and some earache for years. For a few weeks he had noticed discharge.

Seen again in 1930. The little sentinel granulation had grown large enough to obscure the malleus.

Radical mastoid operation June, 1931. Ivory bone; tiny antrum; no erosion of bone, except the malleus; cholesteatoma in the attic.

This case is curious, in having tinnitus as its primary symptom. It illustrates the typical site of perforation and the small amount of disease that one may occasionally find.

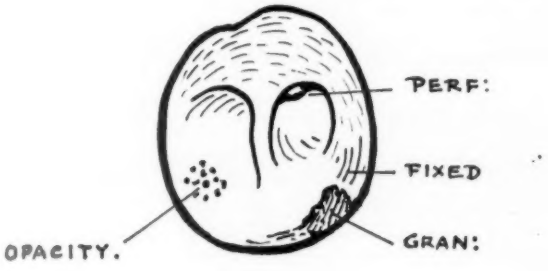


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FIG. 5.

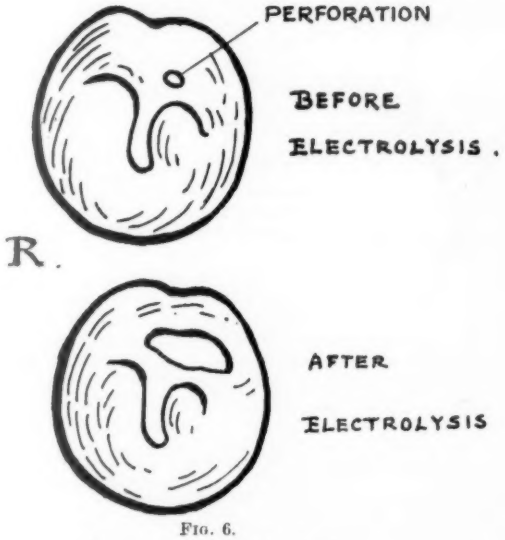


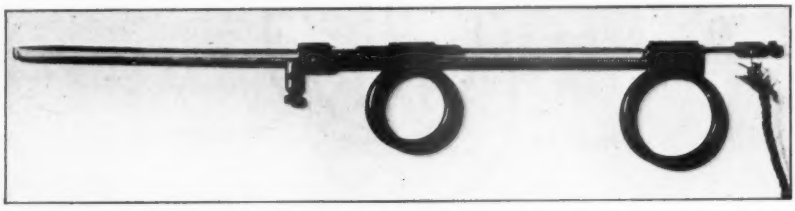
FIG. 6.

FIG. 5.—*Case* 5. E. H. Left.
FIG. 6.—*Case* 6. P. W. L. Right.

Case 5.—E. H., a man aged 25, seen in October, 1930. Slightly deaf since childhood. Discharge from left ear for one year. No headache or giddiness. Membrane showed a tiny track under posterior ligament of malleus, through which fœtid pus can be sucked. There was a small polyp growing from the lower margin of the membrane. This patient has very poor hearing in the right ear. His earning capacity depends on his left ear. He is postponing operation although he realizes his danger.

Case 6.—P. W. L., a man aged 33. Right ear has discharged for twenty years with occasional intermissions. Seen first 4.4.21. Right membrane showed a tiny perforation in Shrapnell's membrane just above the short process of the malleus—the typical site. Thin discharge with fœtor of cholesteatoma. No toxic symptoms.

This case I treated for many months with intratympanic irrigation, antiseptics, ionization, etc., without improvement. In 1923 I enlarged the perforation and attempted to remove the edge of the outer attic wall by Mr. Friel's method. This certainly improved the condition by affording better ventilation for the attic cavity. It remained dry for some months. Discharge has been noticed occasionally up to present date. Hearing on the right is good, although less than normal. The cholesteatoma is evidently of a very mild type in this case.



Friel's instrument for electrolysis of outer attic wall.

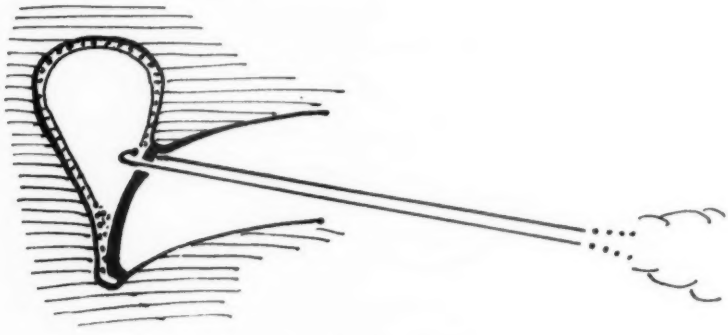


DIAGRAM ILLUSTRATING ELECTROLYSIS OF OUTER ATTIC WALL.

The needle with curved tip is passed through the perforation. The point of the other needle is then advanced until it is embedded in the external tympanic wall. A small portion of this wall now lies between the needle points. A current of 3 or 4 m.a. for ten minutes will destroy the tissue between the needle points.

Case 7.—Miss H. C., aged 50. Right ear shows the so-called "cholesteatoma externa." An excellent imitation of a radical mastoid cavity has been produced by slow absorption of bone. This cavity collects fœtid epithelial débris and has to be cleaned out periodically. The malleus can be seen plastered against the inner wall. On the left side the membrane is dry and fixed to the inner wall—the result of suppuration in childhood. There is considerable deafness of the otosclerotic type. The history indicates that the condition on the right originated in the middle ear.

The following tables give some idea of the frequency with which cholesteatoma is met with in operations on the ear.

The Edinburgh statistics are most thorough and striking. But even in these I surmise that the percentage might have been still higher had cholesteatoma been looked for as a primary condition.

	Hirnabsc. inf. chron. Eiterung	avon cholesteatoma
Heine	29	19 mal—65%
Henke	19	14 mal—74%
Michaelsen	12	9 mal—75%
Nuhsmann	22	14 mal—64%
Ohrenklinik München	8	7 mal—87%

LOGAN TURNER AND FRAZER, EDINBURGH.

Circumscribed Labyrinthitis :—
47 cases : 6 attic perforation or cholesteatoma.
7 cholesteatoma alone, noted previous to operation.
Cholesteatoma found in 39 cases at operation.

Acute Purulent Labyrinthitis :—
14 cases : cholesteatoma noted in 8 previous to operation.

Latent Labyrinthitis :—
16 cases : cholesteatoma noted in 11 previous to operation.

Spontaneous Cure of Labyrinthitis :—
4 cases : cholesteatoma noted in 3.

Extradural Abscess in Middle Cranial Fossa :—
6 cases : cholesteatoma noted in 4.

Extradural Abscess in Posterior Cranial Fossa :—
8 cases : cholesteatoma in 5.

Lateral Sinus Thrombosis :
6 cases : cholesteatoma in all 6.

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Discussion.—Mr. HERBERT TILLEY (after showing two drawings of the anatomy of the tympanic attic for which he was indebted to Professor Schmiegelow of Copenhagen) said: These drawings will, I think, go far towards explaining two of the three questions which Dr. Jobson has asked: Why are "attic" cases so resistant to conservative treatment? In the light of the anatomical conditions which had been demonstrated, surely the resistance must be due to defective drainage, not only between the small areolar cavities in the anterior part of the attic, but also between these cavities as a whole and the freer, undivided portion of the attic posteriorly.

When, for these reasons, suppuration becomes prolonged, chronic osteitis of the immediately neighbouring bony structures sets in, and hence one finds absorption of the heads of the malleus and incus, and of the external attic wall (inner and upper wall of bony meatus), with formation of granulation tissue or polypus formation. At the same time or later on, the infective process finds its way into the freer posterior region of the attic, and thence to the mastoid antrum, and so completes the clinico-pathological picture with which we are all familiar.

It is needless to add that serious complications may arise when the osteitis attacks the roof of the middle-ear cleft or the labyrinthine structures, or lays bare the facial nerve in the aqueduct of Fallopius. Such conditions have their counterpart in chronic suppuration coupled with defective drainage when they occur in the nasal accessory air cavities, and particularly so in the case of the ethmoid labyrinth.

Dr. Jobson's third question is, I think, also explained by the anatomical conditions. The perforation is commonest in the upper region of the membrana flaccida because here it is thinnest, while a band of comparatively thick connective tissue separates the larger upper region of the attic (Kretschman's cavity) from Prussak's space below, where one might otherwise expect to find the perforation. I am on less sure ground in an attempt to answer

his second question with regard to the close connection between attic suppuration and cholesteatomata. My difficulty would be to explain why we never find true cholesteatomata in chronic suppuration of the nasal accessory air cavities where defective drainage is so pre-eminently present and provision for its freedom forms the basis of all treatment.

May not this disparity be due to some developmental characteristics of the attic epithelium not present in that of the nasal cavities? Virchow rather favoured this view and pointed out that the mucous membrane of the attic is the remains of an epidermic "bud" from the external layer of the blastoderm which is buried at the level of the first branchial arch and governs the development of the auditory apparatus of which the aqueductus vestibuli is a normal structure. If Virchow's theory is correct, it would not be difficult to understand that infection of the attic would cause irritation and proliferation of its epithelium which would take the form of the areolar spaces which it lines, ultimately destroy their boundaries and so form the characteristic "cholesteatomatous mass."

I cannot see eye to eye with Dr. Jobson in his theory that cholesteatoma is a primary condition, because there are evidences that it may be caused by an initial tubo-tympanic infection of which I have seen a few instances, and many in which it has followed a primary involvement of the tympanum. Schmiegelow has recorded three cases of primary infection of the attic, one as a complication of influenza, the second following operation for adenoids, and a third resulting from a nasal douche employed during an acute nasal catarrh. Furthermore, Schmiegelow, Bezold and Morpurgo have described cases in which the "bruit de perforation" was heard in purely attic cases; so that it is obvious that infection by way of the Eustachian tube is not so exceptional as one might think.

Nor do I entirely agree with the statement that "one invariably finds the membrane adherent to the inner wall to a greater or less extent." Otologists must often have been struck with the apparently normal appearance of the "membrana propria," especially in comparatively recent cases and also with the relatively good hearing which may be present—an embarrassing condition when one has had to explain to the patient that if a dangerous lesion in the ear is to be removed he must be prepared to find the hearing of the affected ear considerably damaged.

May I suggest that when the tympanic membrane is much indrawn, this may be a result of a primary infection of the tympanum which cleared up but only after it had infected the attic.

With regard the treatment, it has been my experience that if from the history and clinical aspects of the case we can be fairly sure that the condition is of recent origin, it may be possible, by means of Hartmann's cannula, to cure a few cases by daily irrigation and the injection of such solutions as peroxide of hydrogen, argyrol or some of the iodine derivatives. Many more may be cured by ossiculectomy which provides free drainage and access to the attic cavity for the gentle use of a curette and the applications of suitable antiseptics.

In 1891 Ludwig (of Halle) published a record of twenty-eight ossiculectomies. In nine there was no modification of the hearing, in sixteen there was an improvement, and in only three was it made worse. I mention these facts because during recent years there has been a tendency to discount this operation which has a very real and practical value in carefully selected cases, but there will be a still larger residue of cases in which symptoms and clinical findings will lead the experienced otologist to advise an immediate radical operation in order to expose, cleanse, and provide for free and permanent drainage from the tympanic attic and mastoid regions of the middle-ear cleft.

Mr. F. H. DIGGLE said that three years ago he had suggested to a clinical assistant the view that these cases were primary and the rejoinder had been: "That is a very interesting theory, have you written about it? Does anybody believe it?" He had felt it needed someone with a riper experience to put it forward. In the last three years he had had two interesting cases which, he thought, helped to confirm it. Mr. Hamilton would remember the case of a youth in the Army who, during the later part of that career suffered from vertigo. He had a gun-shot through-and-through wound which was below the mastoid region. The man had been regarded as a malingerer and was returned to duty. At the Board he, the speaker, saw that the man had a definite attack of vertigo. Nothing was to be found in the ear, hearing was perfect, and the membrane was normal. He asked the man to continue to attend at the out-patient department and one day a white spot developed over the posterior part of the membrane, and in due course he saw it perforate. A limited

cholesteatomatous disease was seen at operation with a perforation into the external semicircular canal.

The next case had been diagnosed as a simple Bell's palsy, probably of rheumatic origin. One day a small bleb developed on the membrane, in the posterior part of the attic region, and, with the experience of the previous case in mind, he (the speaker) cut down and found a limited cholesteatoma, with necrosis, leading into the Fallopian canal. These cases confirmed his opinion that most cases of cholesteatomatous disease were primary invasions of the attic region.

Dr. Jobson had pointed out the importance of diagnosing these cases early; but he, the speaker, did not know how this could be done; the patients had no pain, no loss of hearing and no discharge at so early a date. It was only by a recognition of the fact that vertigo or even facial palsy, which could not be otherwise accounted for, may, on occasion, be due to an unsuspected limited cholesteatomatous patch in the mastoid bone. Otologists knew the difficulty there was in getting rid of cholesteatomatous material in a mastoid cavity. His chief, the late Sir William Milligan, always made a point in these cases of swabbing out the cavity at the completion of the operation with pure carbolic, with very good results.

Dr. J. S. FRASER said that Dr. McKenzie and Dr. Jobson apparently held that cholesteatoma was a form of congenital tumour due to fœtal inclusion of epiblast in the middle ear. If that was so, it was surely the most frequent form of congenital abnormality which existed in the human race! Cleft palate and dermoid cysts were not nearly so common. He (Dr. Fraser) was convinced that in the majority of cases cholesteatoma was not of congenital origin but was caused by metaplasia. In ozæna, which was the advanced stage of chronic purulent rhinitis, the ciliated columnar epithelium reverted to the squamous type. In chronic bronchitis and bronchiectasis the lining membrane of the bronchiectatic cavity consisted, not of ciliated epithelium but of squamous cells. Cholesteatoma had been produced experimentally in the uterus, and even in the stomach, and in all these regions the squamous cells could not have come from the skin or from fœtal inclusion. Cholesteatoma was a reversion from the more highly developed ciliated columnar epithelium to the lower protective, or squamous, type.

It was a common condition and if all cases were due to the fœtal inclusion of epiblast in the attic and antrum, one would expect that observers like Cheatle and Mouret, who had examined many hundreds of mastoids, would have found a considerable number of specimens showing congenital cholesteatoma formation. So far as he knew, this had not been the case.

Invagination of Shrapnell's membrane might produce a small cavity lined by squamous epithelium. Acute suppuration of the attic due to influenza might become chronic and this also would account for some cases of attic cholesteatoma.

Mr. ALEX. R. TWEEDIE said that he wondered if there was really such a mystery about the condition as Dr. Jobson had suggested. Surely the initial basis of cholesteatoma was, as Dr. Fraser had just indicated, always some infection from the naso-pharyngeal tract. Indeed, the cases shown that day by Dr. Jobson confirmed this view. He (Mr. Tweedie) would submit that the condition was dependent on some primary infection from the nose and throat of the attic or antrum—to which the "owner" offered considerable resistance but only with partial success, so that development of a low form of sepsis continued, and therewith the mucous membrane concerned underwent an abnormal alteration.

Neumann, whom he had quoted in this connection last year, had pointed out that the lining cells of the mastoid cavity were a peculiar form of muco-periosteum, and he (the speaker) suggested that it was the irregular desquamation of this infected epithelium retained by the lack of sufficient means of exit, which was the main factor in the production of cholesteatoma.

With regard to the cholesterin content of the blood, Professor Alex. Rejtö, of Budapest, had already made considerable investigations, as recently reported by himself at a meeting of the "Collegium" in Bordeaux, and also by one of his assistants, in the *Monatsschrift für Ohrenheilkunde*. In this latter communication it was stated that the cholesterin content of the blood had been found fairly constant in normal people; was increased in cases with cholesteatoma, but returned to normal when the latter condition had been successfully treated; that there was no causal relation between the cholesterin content of the blood and the *formation* of cholesteatoma, but that the presence of cholesteatoma, by re-absorption of cholesterin, tended to increase the cholesterin content of the blood. As a further interesting clinical application of these statements, it was then suggested that the degree of the

cholesterin content of the blood might form a valuable indication as to the urgency of a case of suspected cholesteatoma and constitute a reason for operation. With regard to palliative measures, he submitted that oily solutions would be found more efficacious than those with either a watery or spirituous medium.

Dr. ROBERT R. SIMPSON showed the skiagram of a mastoid case. The patient came to the out-patient department complaining of frontal headache, with a foul discharge from the ear. All the membranes and ossicles had disappeared, and the labyrinth was dead. Because of the headache an X-ray examination was made. There was an unusually large cholesteatoma, which had effected a maximum amount of damage without having given much evidence of its presence. There was an erosion of the middle and posterior fossæ, and on removing the cholesteatoma from the sinus and cerebellar dura, some cerebro-spinal fluid escaped. Because of that he, the speaker, thought it wise to delay the completion of the radical operation for forty-eight hours. The external canal was eroded, the facial nerve exposed and the whole promontory gone. He had not suspected any of the complications. There was an extension of the cholesteatoma through the tip deep to the attachment of the sterno-mastoid. After the radical mastoid operation the patient made an uninterrupted recovery. The ear was now, after a year and a half, beginning to discharge again.

Dr. DAN MCKENZIE: The fertilizing nature of the idea that cholesteatoma is always primary is to be seen in Dr. Jobson's paper, for by it the attention of the surgeon is directed first and foremost, though not by any means exclusively, to the epidermal sheet that is responsible. The grasping of this truth—as I believe it to be—was the most important practical point in my recent paper. The further discussion on the origin of the cholesteatomatous lining is more or less academic, nevertheless it is of great interest.

There is, as I said a year ago, much to be said for the metaplasia theory; on the other hand, there is much also to be said against it. To begin with, how does it come about that only a fraction of those who suffer from suppuration of the middle ear develop it? And yet, compared with cholesteatoma in the nose and its sinuses, in the gall-bladder, in the uterus, and so on, cholesteatoma in the ear is extremely common. It can scarcely be due simply to metaplasia in an enclosed space, or we should find it common also in sinusitis of the frontal and ethmoid bones. As to the relationship of ozæna with cholesteatoma no one can deny that, in both, the essential pathological condition is the presence of stratified keratinized epithelium where it has no business to be. But the change in ozæna is general, implicating the whole of the respiratory tract, down to and including the larynx and sometimes even the trachea. On the other hand, as I pointed out in my former paper, aural cholesteatoma is curiously localized and circumscribed; it presents a nidus. Further, we seldom, very seldom, find aural cholesteatoma associated with ozæna. When the ear goes wrong in ozæna, it is usually dry otosclerosis, or a tubo-tympanic suppuration.

Recurring to the metaplasia theory, we must remember that whatever theory we adopt, it will have to explain the predilection shown by cholesteatoma for the attic-antrum region; and the metaplasia theory is weak in this respect. True, in my former paper I suggested that, as the lining of the tympanum consisted mainly of cubical cells at this part, it was conceivable that their transformation would be more easily effected than if they were cylindrical. But this is pure hypothesis. We know that cylindrical epithelium changes into stratified epithelium readily enough. Why then should the metaplasia from suppuration be confined to the attic and antrum? Why does it never appear in tubo-tympanic suppuration? And if cholesteatoma were due to simple metaplasia in a confined space, why do we not see it as an everyday occurrence, as often as scar tissue forms in a suppurating ear? There is no answer to these questions, and until there is we must regard the metaplasia theory as dubious.

Let us turn now to the possibility of congenital implantation. By way of interest I show here a photograph of the lining of an ordinary implantation cyst, for permission to use which I am indebted to Professor Muir. Its resemblance both to aural cholesteatoma and to the cholesteatomatous brain tumour leaps to the eye.

I do not propose to recapitulate what was said in my former paper on this subject. I will merely add a few points in its favour that have since occurred to me. When we examine the course of development of the external auditory meatus and tympanic cavity, the likelihood of congenital implantation through the detachment of epidermal cells cannot be denied. For,

we are here looking at a peculiar—a unique—structure. Nowhere else in the body does the subcutaneous tissue form the periosteum as it does in the roof and posterior wall of the deep meatus. That is to say, nowhere are skin and bone so closely, so intimately, connected. You might even call them contiguous. Again, in Shrapnell's membrane you have this fine skin-layer unsupported by bone, in contact with tympanic epithelial lining.

Now this arrangement is due to the invasion during fœtal life of the mesenchyme by a solid plate of ectodermal cells, sprouted off from the primary external auditory meatus, which pushes in through solid mesenchyme to form the deep meatus, hairless and devoid of glands; to form also, with the mesenchyme and the endoderm, the tympanic membrane, and finally, though not actually until after birth, Shrapnell's membrane. During this invasion, be it remembered, the only hard structures the meatal plate encounters are the handle of the malleus and the tympanic ring, both of them cartilaginous. Obviously, nothing is more

Implantation cyst. Source not stated. They occur on cutaneous integument and conjunctiva. (From Professor R. Muir's *Textbook of Pathology*. With grateful acknowledgments.)

probable than that in its penetration and expansion to form the deep meatus, the meatal plate should shed a cell here and there, which, sequestered and enclosed by the later developing bone of the outer attic wall and of the bony meatus, would form the starting point of an epidermoid—a congenital implantation cyst.

But, it may be objected, if this were to occur, surely evidence of such epidermal rests ought to be found in these regions. This objection can be met. Such rests have been found and reported, under the picturesque name of epidermal "splinters," and their significance relative to the development of primary cholesteatoma has been recognized.[1]

Let me remind you also of the cholesteatomatous cyst of the membrane I depicted in my paper. Finally, I should like to say that this theory explains also the small dry puckerings, depressions, and even tunnels or fistulæ so frequently seen in Shrapnell's membrane.

We are therefore entitled to suppose that the congenital implantation cyst is probably quite a common event.

Before concluding, I should say that my attention has been drawn to the report of aural cholesteatoma by invasion being successfully and artificially produced in animals. Unfortunately, the reports available have been so scantily detailed that I am unable to express any opinion upon them, whether critical or otherwise. They certainly seem to have been accepted by well-known authorities. But authorities occasionally err, as Politzer did over Kirchner's Haversian invasion.

I saw recently a statement made by a prominent authority to the effect that cholesteatoma could form in acute suppuration of the middle ear in two or three days even in the scarlatinal form by invasion. This is incredible. Politzer said that cholesteatoma, under those circumstances, did not occur, acute sepsis rendering such an event impossible. We know with

[1] Precechtel. Acta O-L. xiv. Fasc. 1-2.

what difficulty the normal epidermis extends over an inflamed ulcerated surface, and yet we are to believe that in the presence of acute scarlatinal suppuration of the middle ear, in spite of the intensity of the infection, it is possible for the epidermis to invade the tympanic cavity. I find it difficult to believe that at one and the same moment the epidermal covering of the membrana tympani dies, forming the familiar white pellicle found in this condition, and also manifests so much increased vitality that it can make a victorious invasion of the middle ear.

Dr. JOBSON, in reply, said he thought that there was something operative besides pressure, namely, the absorptive power of cholesteatoma.

One met with cases of pseudo-mastoid cavity, such as Case No. 6, showing in the other room, in which there was no pressure at all; there was simply a layer of epithelium which absorbed bone and had produced the cavity. That had gone on year after year and caused the condition. He agreed, however, that pressure had an effect in some cases.

Mr. Tilley accounted for the obstinacy of the cases by the very complex topography of the cavity of the attic. True, but that was common to all cases of suppuration; it was common to cases of ordinary tympanic sepsis with a perforation in the lower tympanic membrane, as well as cholesteatomatous cases. But the difference in behaviour in these two groups of cases was very striking. When one met with a fair-size perforation in the lower tympanic membrane, one could almost guarantee that the ear would clear up and the sepsis would abate. In both cases, however, the sepsis involved the attic, the only difference being that there was a different type of epithelium lining the attic in one case as compared with that in the other, this accounting for the chronicity and the obstinacy.

He was aware that Dr. Fraser's argument was very strong, that if cholesteatoma was called a congenital tumour it was the commonest of all forms; but if one called it by another name, congenital epithelial defect, the hypothesis of Dr. McKenzie became more acceptable.

THE FOLLOWING ILLUSTRATIVE CASES WERE SHOWN.

Cholesteatoma Exposing the Lateral Sinus.—SOMERVILLE HASTINGS, M.S., F.R.C.S.

L. H., a woman aged 47, was shown at a meeting of this Section in November, 1917. She gave a history of chronic discharge from the right ear for eight years, and a pain in that ear of a few weeks' duration. She said that she had never had any operation on the ears. The right ear was filled with pus and epithelial débris and when this was removed a smooth-walled cavity was exposed, all trace of the membrana tympani and ossicles being lost. The walls of this cavity were ulcerated in places, and posteriorly, for about half an inch, the lateral sinus was exposed and could be seen pulsating. The hearing in the right ear was then very defective and no tuning fork could be heard by air conduction, but middle and lower tones were heard by bone conduction, with a noise machine in the left ear. There was much scarring of the posterior wall of the pharynx which was said to be the result of scarlet fever when in childhood.

The patient attended hospital at rare intervals until July, 1930, when she was admitted urgently with a history of hæmorrhage lasting several hours, from the right ear. When blood-clot was removed, a tiny ulcer over the site of the lateral sinus was visible, but no hæmorrhage took place while the patient was in hospital. The small ulcer rapidly healed but no pulsation has been visible in the lateral sinus since this incident. Since July, 1930, the patient has attended hospital three or four times for removal of epithelial débris from the ear, but there has been no ulceration.

Cholesteatoma and Epithelioma: Specimen.—DAN MCKENZIE, M.D.

In a paper read before the Section last year mention was made of the possibility of transformation of cholesteatoma into epithelioma. The present sections are from a case in which the two were present in association.

Healed Marginal Perforation of Posterior Half of Membrana Tympani: Specimen.—E. D. D. DAVIS, F.R.C.S.

Cholesteatomatous suppuration of the attic with a fistula of the ampulla of the external semicircular canal.

The patient was admitted with a temperature of 104°, drowsy and too ill for labyrinthine tests. At a mastoid operation, a late lateral sinus thrombosis with an extensive abscess was found.

The patient died from cavernous sinus thrombosis.

Twelve months before death there was a history of severe vertigo.

Cholesterol Metabolism.

By JOHN ADDYMAN GARDNER, M.A.

(Reader in Physiological Chemistry and Biochemist, St. George's Hospital.)

THE one certain conclusion that can be drawn from the very large amount of work done on this subject during the past fifty years is that cholesterol is an essential constituent of every cell of the body, just as are protein, fat and carbohydrate. It is present in all body fluids; even urine contains traces, much augmented in albuminuria. Chemically, cholesterol is an unsaturated secondary alcohol with one doubly-linked pair of carbon atoms. It exists in the body in the free or alcoholic condition, and also in the form of its esters with the higher fatty acids—oleic, palmitic and stearic acids. These two forms are not equally distributed. Brain and the red blood-corpuscles, for example, contain it almost entirely in the free state. Two samples of moist adult human brain contained respectively 1·95 and 1·91% of cholesterol, but no cholesteryl esters; the brain of a three-months old child 0·69%, all free; average for brain of three still-born children, 0·56 free and 0·006% ester, and a fœtus (5 to 6 months) 0·44 free and 0·009 ester.

Analyses of five samples of moist human red blood-corpuscles gave an average of 0·074% free cholesterol, with individual variations of 0·062-0·081, and 0·003 cholesterol as esters.

In human bile the percentage of cholesterol is very variable, but mainly in the free condition, and probably in close association with bile acids.

Other tissues contain both free cholesterol and cholesteryl esters. For example:—

GRAMMES OF CHOLESTEROL PER 100 GRAMMES OF DRIED NORMAL ORGAN. (*Fex.*)

Organ	Total cholesterol		Free cholesterol		Ester cholesterol	
	Average	Limits of variation	Average	Limits of variation	Average	Limits of variation
Liver	1·283	0·96— 1·55	1·024	0·71—1·31	0·258	0·17— 0·32
Kidney	1·661	1·37— 2·01	1·540	1·14—1·91	0·109	0·06— 0·15
Suprarenal (whole) ...	16·187	10·71—19·98	2·611	1·40—3·00	13·800	7·98—17·35

In the above table the "cholesterol" is, strictly speaking, the sterol precipitable by digitonin in the form of a digitonide insoluble in alcohol and ether. This sterol is in fact mainly cholesterol, but as Schönheimer has recently shown may contain small quantities—2 to 4% of the whole—of a saturated sterol, viz., bihydrocholesterol, which is also precipitable by digitonin.

In studying the metabolism of the human subject, attention has been mainly directed to the blood and excreta, since other organs can only be dealt with post mortem.

In the red cells, where the cholesterol is mainly in the free condition, the percentage appears to be fairly constant both in health and disease. On the other hand, the cholesterol of the plasma changes markedly during both the ordinary metabolic processes and in disease. This variation takes place, in healthy metabolism, mainly in the ester portion. For this reason it is *essential* that blood cholesterol estimations should be done on the plasma, or at any rate on the serum, so that changes in the cholesterol content should not be masked by the rather high constant mass of corpuscular cholesterol; and further, that the interpretation of results should not be complicated by the presence of anæmia.

It is very important that both free and ester cholesterol should be estimated, otherwise we get only a part of the story, and often the less interesting part.

During the past twenty years a vast amount of work has been published on the amount of cholesterol in the blood in disease. Unfortunately, in earlier years most writers dealt only with the total cholesterol, and even at the present day we find too many workers doing the same, as though they regarded the esterification as merely fortuitous. This unfortunate position may be explained by the historical development of the subject. The ether extract of tissue contains fatty acids, fats, cholesterol, cholesterol esters, &c., a mixture often lumped under the misleading and undefinable term—lipoids. In early days the separation of these constituents presented many difficulties, and their association led to the idea that cholesterol is intimately connected with fat metabolism—a view in support of which there is little real evidence. This idea has persisted, however, and has been largely insisted on by the French school of observers.

Space does not, however, permit of a discussion of the various theories that have been propounded on sterol metabolism, and indeed at the present time we have not got the data on which to base a really sound theory, or even effectively to criticize hypotheses propounded from time to time. I propose, therefore, simply to draw attention to certain biochemical facts, accumulated during the past decade, which must be taken into account in any proper interpretation of results.

(1) It is important to realize at the outset, in dealing with hypercholesterolæmia in disease, that in health the range of plasma cholesterol values is considerable. The following figures are the result of examination of about fifty normal individuals of both sexes:—

GRAMMES OF CHOLESTEROL PER 100 GRAMMES OF PLASMA.

	Total cholesterol		Free cholesterol		Ester cholesterol	
	Average	Limits of variation	Average	Limits of variation	Average	Limits of variation
Males	0·170	0·11—0·22	0·050	0·005—0·082	0·12	0·08 —0·14
Females ...	0·153	0·08—0·23	0·054	0·02 —0·094	0·10	0·054—0·14

It will be seen, at a glance, how wide is the range of normal values in different individuals, but in actual fact the level of plasma cholesterol in a single individual is much more constant, and the writer has records of his own plasma cholesterol, taken fasting, over several years, which show but little variation.

The ratio of ester cholesterol to the total cholesterol in the plasma is in the majority of cases between 60 and 70 per cent. It should be noted that the cholesterol and cholesterol esters in plasma are not simply present in colloidal solution or suspension, as such, but, as the writer and Gainsborough have clearly shown, are in intimate physical or perhaps loose chemical union with the proteins, particularly the globulins.

(2) In the past decade the purely chemical investigation of cholesterol, due largely to the labours of A. Windaus and H. Wieland and their co-workers, has gone far ahead of the physiological or medical side.

Cholesterol, an unsaturated secondary alcohol of the formula $C_{27}H_{46}O$, is derived from the parent saturated hydrocarbon, cholestane $C_{27}H_{48}$, whose molecule consists of

four conjugated hydro-aromatic rings (two six-carbon rings and two five-carbon rings) and an octyl side chain.

Various artificial isomers of cholesterol have been prepared in the laboratory, perhaps the most interesting being the very labile *allocholesterol*, in which the position of the double linkage is changed. It is very readily changed back into ordinary cholesterol. This allocholesterol is very easily reducible in vitro to coprosterol. In adult man the waste cholesterol of the body is mainly excreted through the intestine, for the most part as a mixture of isomeric alcohols, $C_{27}H_{48}O$, viz., bihydrocholesterol and coprosterol, the latter in preponderating quantity. Bihydrocholesterol is the natural reduction product of cholesterol, produced by saturating the double link with hydrogen. In the formation of the isomeric coprosterol, a steric rearrangement of the substituent groups at a particular carbon atom has occurred in addition, and the parent hydrocarbon is coprostane, a stereo-isomer of cholestane. The formation of coprosterol is generally believed to occur in the gut and to be due to reduction of cholesterol by intestinal bacteria, but the evidence for this is not too convincing.

The specific bile acids and cholesterol possess the same carbon structure, except that in the bile acids an isopropyl group $(CH_3)_2CH$ has been eliminated from the side chain and the carbon atom, to which it was attached, oxidized to a COOH group.

It is clear from this work that the sterols and bile acids form a group of substances of analogous structure, which is entirely different from that of the usually considered metabolic groups such as proteins, carbohydrates or fats. The bile acids that have been most thoroughly studied are those of ox-bile, viz., lithocholic acid, $C_{24}H_{40}O_3$, deoxycholic acid $C_{24}H_{40}O_4$ and cholic acid $C_{24}H_{40}O_5$, which are hydroxyl derivatives of the parent acid, cholanic acid $C_{24}H_{40}O_2$. In goose, ox and human bile another deoxycholic acid, with the two hydroxyl groups in another position, is also found, viz., cheno- or anthropodeoxycholic acid. These acids, though they occur as such in bile, are usually coupled with glycine or taurine. They belong to the same stereo-isomeric series as coprosterol, whose parent hydrocarbon is coprostane. However, from pigs' bile a hyodeoxycholic acid has been isolated, and it is the only naturally-occurring acid, so far found, which belongs to the same stereochemical series as cholesterol. The following scheme shows their relationship:—

Parent hydrocarbon	Cholestane	Coprostane
Unsaturated alcohol	Cholesterol ⇄	Allocholesterol
Saturated alcohol	Bihydrocholesterol	Coprosterol
Bile acids	Hyodeoxycholic acid	Various derivatives of cholanic acid

It is important to note that in vertebrate animals the only sterol isolated, with the exception of small amounts of its reduction product bihydrocholesterol, and traces of ergosterol or an alcohol very like it, is common cholesterol; whereas many different bile acids have been isolated from different species of animals. Furthermore, in the different animals the acids, even though the same, are present in very different relative proportions.

On account of the close chemical relationship between bile acids and cholesterol, it has been suggested by Windaus that the bile acids are formed by direct breakdown of cholesterol in the organism. Enderlen, Thannhäuser and Jenke found that intravenous injection of cholesterol in colloidal solution produced no increase in the secretion of bile acid, whereas similar injections of allocholesterol led to noticeable increases of this secretion. The result is significant, but unfortunately the available methods of estimating bile acids are indirect and unsatisfactory, and afford no information as to the relative distribution of the different acids. On the other hand, since Wieland succeeded in synthesizing coprostane from cholanic acid, the reverse

change appears possible. In the writer's opinion, however, a close consideration of the formulæ assigned to these substances suggests that both cholesterol and bile acids are synthesized from some common origin by collateral processes.

(3) In 1916 H. Wieland and S. Sorge enunciated the "choleic acid principle"; they found that deoxycholic acid formed stable molecular compounds with the higher fatty acids, e.g., $8C_{24}H_{40}O_4 + C_{18}H_{36}O_2$ with stearic acid. The choleic acids isolated from bile were a mixture of such stearic, palmitic and oleic acid compounds. These compounds go unchanged into the salt condition and are very stable. They crystallize well and their sodium salts are *very easily soluble in water*. Besides fatty acids, these observers found that many other substances form somewhat similar compounds with deoxycholic acid, though often more easily dissociable. Materials which are insoluble, or nearly so, in water, such as naphthaline, xylene, strychnine, quinine, cholesterol, camphor, fat, etc., are brought into solution by an aqueous solution of sodium deoxycholate. This power of uniting with insoluble substances to form soluble products Wieland called the "choleic acid principle," and suggested that it had an important function in transporting insoluble substances, such as fat and fatty acids, etc., through the intestinal wall.

It is perhaps important, in connection with cholelithiasis, to note that anthropodeoxycholic acid, isolated from human corpse bile, in which it accompanies ordinary deoxycholic acid, *does not obey* the "choleic acid principle."

This choleic acid principle appears to provide a more satisfactory explanation of intestinal fat absorption than either the theory of particulate absorption or that of the absorption of fatty acids in the form of soluble soaps.

(4) Ox bile has long been known to have a cholagogue activity when given by the mouth. Recent investigations have shown that deoxycholic acid possesses marked cholagogue activity in animals and man, and also that the corresponding keto acid, which can be administered intravenously, is even more potent.

(5) That cholesterol is synthesized in the organism has been clearly proved by balance experiments by Gardner and Fox, and by Thannhäuser, and in other ways by Beumer and Lehmann, H. G. Channon and others.

(6) Cholesterol ingested with the food is absorbed by the alimentary canal, but in this respect the metabolism of herbivora appears to differ very markedly, in degree if not actually in type, from that in carnivora or omnivora.

In the herbivora, ox, sheep, horse, rabbit and hippopotamus—Gardner and other workers have clearly shown that cholesterol is never excreted in the fæces of the healthy animals; and the writer was led to the conclusion that, in the metabolism of these animals, cholesterol is strictly conserved. Evidence was brought forward to show that the cholesterol excreted in the bile, including such as arises from the breakdown of erythrocytes, is completely reabsorbed—the so-called "cholesterol cycle." In such animals, any waste of cholesterol must be made up by synthesis. Before this possibility was proved, many attempts were made by Gardner and others to ascertain whether the vegetable sterols of plants could be absorbed and converted into cholesterol, but the results were inconclusive, owing to the then lack of information as to the variations of cholesterol in normal animal blood. It was shown, however, that the so-called chortosterol of grass was excreted unchanged and practically quantitatively. This chortosterol is, however, possibly not a sterol, but a paraffin alcohol. In recent times, Schönheimer and co-workers have been able to demonstrate that plant sterols, ingested in known quantities in the food, are quantitatively excreted, and in tissues behave as foreign bodies, but on the other hand cholesterol, so administered, is very rapidly absorbed. In herbivora the administration of cholesterol, which is not a normal constituent of their food, leads to toxic effects. Prolonged feeding of this substance to rabbits, as is well known, leads to cholesterol infiltration of the various tissues, the changes in which have been considered to resemble human pathological processes, e.g., athero-sclerosis.

In carnivora and omnivora an excretory mechanism appears to exist, so that

always a quantity of sterol is excreted in the fæces. This may be cholesterol or coprosterol or both, together with a small amount of bihydrocholesterol. In adult man the bulk of the excreted sterol—80% or more—consists of coprosterol. The rest is made up of bihydrocholesterol, which appears to be excreted through the intestinal walls, and cholesterol. The quantity of sterol excreted is always greater in quantity by almost 0·3 grm. per day than the cholesterol ingested with food. In infants, however, in the milk stage only cholesterol is excreted, and there is only a very slight excess of output over intake, almost within the errors of experiment. At what stage and under what conditions this gives place to coprosterol is as yet unknown.

This change of cholesterol to coprosterol, as was suggested several years ago by the writer, may be one of the factors which limit the absorption of cholesterol. In this connection it is significant that, as Schönheimer has shown, coprosterol administered with food is not absorbed, and in tissue behaves as a foreign body.

However, in carnivora there is no doubt that cholesterol is absorbed from the food and reaches the blood-stream in partially esterified form through the lymph, though some may enter the portal circulation directly. In carnivora and omnivora no one has ever produced by high cholesterol feeding such pathological phenomena as occur in rabbits.

(7) In man, as in other animals, e.g. cats and rabbits, the level of the cholesterol content of the plasma, taken fasting (i.e., before breakfast), can be raised or lowered by *sufficiently* prolonged feeding with diets of high or low cholesterol content. Such changes are most marked as regards the cholesterol in ester form. As a result of a single meal, alimentary hypercholesterolæmia in the ordinary accepted sense does not occur, and there is no obvious connection between the amount of cholesterol ingested and the cholesterol level of the plasma during digestion. During the digestive process, changes in the cholesterol content of plasma frequently occur, sometimes in a positive and sometimes in a negative direction compared with fasting values. Often a temporary disturbance of the ester to total ratio is observed. These peculiar changes cannot be explained by the influx of cholesterol absorbed from the alimentary canal, but are evidence of an active endogenous metabolism, in which cholesterol takes part, during digestion.

Apart from the changes just mentioned, the only physiological condition in which the value of the plasma cholesterol is altered markedly is in pregnancy. In this condition, from about the twentieth week, the free cholesterol increases to a maximum which it reaches about the thirtieth week, and concurrently the ester cholesterol falls to a minimum. From this time the amount of free cholesterol decreases and the ester increases till an almost normal ratio of free and ester cholesterol is reached before or near parturition. The plasma cholesterol values usually become quite normal in the first or second week of the puerperium.

This characteristic picture has, so far, not been explained.

Cholesterol level in certain pathological conditions.—In numerous papers in medical literature hypo- or hyper-cholesterolæmia has been stated to occur in a large variety of disease conditions, but in very many of the cases the changes noted have been really within the limits of normal variations.

Hypocholesterolæmia certainly does occur, but at the height of the fever only, in a variety of febrile and infective conditions, but the meaning of this is not yet understood.

True hypercholesterolæmia occurs in certain types of nephritis; hypothyroidism, biliary stasis and diabetes.

Nephritis.—Hypercholesterolæmia is present in all those cases which possess the "nephrotic" syndrome, marked by diffuse parenchymatous degeneration, heavy albuminuria, changes in the plasma proteins, and where œdema is the chief symptom. Consequently increases of plasma cholesterol are found in these cases of acute nephritis of prolonged duration, when albuminuria is persistent and hæmaturia absent, and, as Gainsborough has pointed out, in all that group of chronic nephritis

which includes, at one end of the scale, the so-called pure "nephrosis," and at the other end, cases of parenchymatous nephritis in which the initial "nephrosis" is more or less rapidly followed by sclerosis and contraction of the kidneys. The total cholesterol in the plasma may reach as much as 1%, and the percentage of total in form of ester may assume abnormal value in either direction. This high level of cholesterol is present throughout the course of these cases of nephritis, so long as there is any tendency to œdema, and it persists in cases of subacute parenchymatous nephritis for long periods, even though œdema is temporarily absent. After a more or less prolonged period the tendency to œdema is replaced by tendency to vascular changes, increase of blood-pressure and signs of nitrogen retention, and about the same time the hypercholesterolæmia diminishes.

Hypercholesterolæmia is not found in cases of interstitial nephritis or in arterio-sclerotic kidney or in arteriosclerosis.

The cause of this hypercholesterolæmia is not known, but may perhaps be related to the disturbance of the plasma proteins resulting from proteinuria.

Myxœdema.—The total cholesterol of the plasma in this condition may be as much as 50% above normal, but after administration of thyroid gland the value generally approaches normal.

Biliary stasis.—Hypercholesterolæmia has been stated to occur in cholelithiasis and in affections of the liver, but there can be little doubt that, in all the earlier investigations, the hypercholesterolæmia noted was due to the biliary stasis, and not to the pathological condition prior to this. Hypercholesterolæmia is not a feature of uncomplicated cholelithiasis. If, however, biliary stasis occurs, e.g., from impaction of a stone in the common bile-duct, or from catarrhal jaundice, the blood-picture shows very interesting changes. In the early stages the cholesterol ester rapidly diminishes and may almost disappear from the plasma, while the free remains normal or shows a slight increase. This characteristic change of the plasma cholesterol may also be observed in those cases of cholecystostomy where none of the bile is reaching the intestines.

This change must be due to the disturbances of fat and cholesterol absorption from the intestines, consequent on the absence of bile.

If complete biliary obstruction persists for many weeks, then the plasma cholesterol gradually increases, both in free and ester forms, until marked hypercholesterolæmia occurs, but nevertheless the percentage of total cholesterol as ester remains low and is usually from 30 to 40%.

If the biliary obstruction is not quite complete or is intermittent, the marked hypercholesterolæmia may not appear.

Diabetes.—True hypercholesterolæmia sometimes occurs in severe cases of diabetes.

Hypercholesterolæmia in diabetes and also in biliary obstruction may lead to deposition of cholesterol in the skin as xanthoma.

Skin.—Our knowledge of the biochemistry of skin is very defective, but there can be little doubt that it is one of the minor paths for cholesterol excretion. Cholesterol, cholesterol esters and bihydrocholesterol have been isolated from skin and skin secretions. Earlier investigators stated that in human skin no lanoline was present—mainly on histological grounds. Lanoline, the fat of sheep's wool, has been subjected to much investigation. In addition to cholesterol and cholesterol ester and various fats, it contains a substance called isocholesterol, which was supposed to be an isomer of cholesterol, and was also said to occur in latex of certain rubber plants. It belongs to the group of sterols which do not form insoluble compounds with digitonin. Recently Windaus has shown that this isocholesterol is not a single substance, but consists of two sterols, crystallizing together like a single substance, which he names agnosterol and lanesterol. Agnosterol contains three double linkages and lanesterol two; and moreover their molecules contain thirty carbon atoms, and not twenty-seven, so that they are not simply related to cholesterol.

Clearly, skin will repay closer investigation, though the subject is beset with difficulties.

Section of Physical Medicine.

[*December* 18, 1931.]

The Energy Exchanges in Muscle and Nerve.

Samuel Hyde Memorial Lecture.

By A. V. Hill, F.R.S.

The liberation of energy at rest.—All living tissues liberate energy continuously, even when apparently completely at rest, presumably in maintaining the state of readiness to respond to a stimulus, which is a characteristic property of life. If, so to speak, the engine is to be ready to develop power immediately when called upon, it must be left "ticking over" even when no power is actually being taken from it. This resting energy liberation depends upon the temperature, increasing in rate two to three times for a rise of 10° C. It is about the same per gram in muscle and nerve, namely, at 20° C. about 4×10^{-3} calorie per gram per minute, which would correspond, were there no heat loss, to a rise of temperature of about 4×10^{-3}° C. This value refers to muscle and nerve in oxygen. In the absence of oxygen the tissue gradually becomes asphyxiated; its heat production, however, is not reduced to nothing, but to about one half. The process involved in this case is probably chiefly the formation of lactic acid from glycogen, the anaerobic process which appears so frequently to occur when oxidation for some reason or another is prevented.

The effect of temperature on the resting metabolism, whether in oxygen or in its absence, may be expressed in another way, namely, that a 10% increase (or decrease) occurs per 1° C. rise (or fall) of temperature of the tissue.

Energy liberation during activity. Absolute values.—Although at rest so alike in respect of their rate of energy liberation, muscle and nerve differ enormously during activity. The maximal activity of muscle increases its metabolism, say 500 times; the maximal activity of nerve increases its metabolism by, say, 25%. To make a nerve give out as much extra heat, as the result of stimulation, as is given out by a muscle in a single twitch, it is necessary to stimulate it for about five minutes at maximal rate. In a muscle a single twitch gives a rise of temperature of about 0·003° C., and a 1 sec. tetanus of a frog's muscle at 20° C. gives a rise of temperature of about 0·03° C. These numbers refer to contraction and relaxation alone. Following these primary processes is a secondary one called recovery, lasting for ten minutes or more (according to the temperature, the amount of exercise and the oxygen supply), in which a further amount of heat is set free about equal to that in the "initial" processes of contraction and relaxation. In the absence of oxygen a muscle is fatigued in a few seconds of maximal effort, and it regains its full power of contraction only after a prolonged period of recovery.

In a nerve, on the other hand, a single impulse travelling along it causes an initial rise of temperature of only about two one hundred millionths of a degree C., i.e., 2×10^{-8} °C. In a recent experiment I found that half a second of maximal stimulation caused a rise of temperature of $1 \cdot 4 \times 10^{-6}$ °C. during the stimulus and a further rise of $4 \cdot 5 \times 10^{-6}$ °C. during the next 5 sec. In nerve the recovery heat

is relatively enormously greater than in muscle. In muscle the recovery heat is about equal to the initial heat; in nerve it is apparently forty or more times as great. The recovery process goes on for 10 min. to an hour after stimulation, and it uses oxygen, either in the molecular form obtained by diffusion, or from some mysterious oxygen store, not yet properly understood, contained in the tissue itself.

Corresponding to its very small liberation of energy during activity a nerve in oxygen is not appreciably fatigued, even in a maximal tetanus lasting for half an hour or more. This refers to the case of medullated nerve; in non-medullated nerve there is evidence that the energy liberation is much greater and fatigue correspondingly sets in more rapidly.

The several phases of energy liberation.—When a muscle contracts, energy is set free: (*a*) in setting up the contraction, that is in developing mechanical potential energy available to do work; (*b*) in maintaining the contraction, i.e., in keeping up the state of high potential energy; (*c*) in relaxation when the mechanical potential energy is dissipated; (*d*) in recovery.

The recovery process will be referred to again later. Full recovery necessarily involves the use of oxygen, but the discoveries of the last two years have made it clear that partial recovery can go on without any oxygen at all.

In nerve the energy is liberated, so far as we can say at present, only in two phases: (*a*) in the impulse proper, which we may describe as a "propagated electro-chemical change" of some kind; (*b*) in recovery, during which the electrical potential differences discharged during (*a*) are restored.

The full recovery process again involves oxygen, but in the absence of oxygen apparently, recovery can still proceed for some time, as stated above, at the expense of some oxygen reserve. Presumably Nature does not wish to take any risk, and provision is made by which a nerve can function, apparently normally, for some time, even when no molecular oxygen can reach it. Finally, of course, it becomes asphyxiated and refuses to work, but if oxygen be admitted to it again it rapidly recovers and absorbs an excess of oxygen to make up for what was lacking during the previous time.

The maintenance of muscular contraction.—In ordinary voluntary muscle the maintenance of a prolonged contraction is very expensive, as everyone knows who attempts to hold a weight for some time at arm's length. The expense is reduced by *any* change which renders the contraction less rapid, e.g. (1) by a fall of temperature, (2) by previous activity, (3) in some muscles by carbon dioxide.

An obvious method of maintaining a contraction less expensively is to employ a slower muscle for the purpose, and many muscles contain fibres of different size, some presumably for rapid twitches, others for less expensive maintained contractions. Smooth muscles, being very slow, maintain a contraction with very little expense.

The way to picture the relation between speed of contraction and economy of maintenance is to think of every muscle as having a time scale of its own, of working, not in our units of time but in its own "local" time, which we may regard as measured by the time necessary for a single twitch. This "local" time scale is not constant for a given muscle; it depends upon its temperature, upon its chemical environment, and particularly upon the amount of its previous activity. A very striking adaptation in this respect has recently been studied. When a muscle is stimulated, long before fatigue sets in, it begins to show a progressive lengthening out of its contraction in successive twitches. Even the gastrocnemius of the frog, at any rate of some frogs under some conditions, may so rapidly alter its time scale that the tenth twitch of a series at 1 or 2 seconds intervals may take two or three times as long as the first. Half a minute of rest causes a reversal of this spreading out of the contraction, the initial speed being entirely or almost regained. This change of time scale as the result of activity is obvious enough, now one comes to explore it, even in the skeletal

muscle of vertebrates, but in other muscles, with which the general physiologist often deals, it is a most striking, almost a dramatic, phenomenon. The claw muscle of the crab, the retractor of the œsophagus of the snail, the adductor muscles of shellfish, all rapidly become slowed as the result of activity, with the very important consequence that they can maintain a contraction for long periods at comparatively small expense. This beautiful adjustment enables them on the one hand to be quick, or comparatively quick, for the initial stage of contraction, and then allows them to maintain a force for long periods without becoming exhausted. The mechanism of this effect is not understood, but it is being actively explored.

The source of energy in muscle.—Up to a very short time ago a muscle was supposed to derive its energy during contraction from the breakdown of glycogen to lactic acid, the process being reversed with the liberation of further energy by oxidation during "recovery." Just five years ago Eggleton and Eggleton discovered a new compound in muscle, namely "phosphagen," i.e. creatine phosphoric acid, and in the last year particularly, this substance has ousted lactic acid from its primary place in our theories of muscular contraction. It had long been known that creatine is present in comparatively large amounts in skeletal muscle, but no function had been allotted to it; and for many years phosphoric acid and its esters had been known to play some unknown rôle. It seems now that when a muscle contracts the energy required is liberated by the breakdown of creatine phosphoric acid into its constituents. As soon as the contraction is over, this breakdown tends to be reversed by one or other of two means: (i) By the energy liberated in the breakdown of glycogen to lactic acid, and (ii) by oxidation occurring slowly in recovery, which also reverses the glycogen lactic acid breakdown.

The main facts about lactic acid still remain much as they were and as they are found in the textbooks, but the time relations of its liberation are now known to be different. The lactic acid is liberated *after*—and not *during*—the contraction; the energy of its liberation does not supply the energy for contraction but that for the reversal of the other process which did supply the energy for the contraction. Such of the phosphagen breakdown as is not reversed by subsequent lactic acid formation is reversed during oxidative recovery, and its reversal has a prior claim on the energy liberated in that. The rest of the energy of combustion is used either to reverse the glycogen lactic acid breakdown or is wasted as heat.

Fatigue and rigor.—Fatigue and rigor were attributed until recently to the accumulation of lactic acid. It is now known, however, that muscles can be completely fatigued and may go into rigor without any lactic acid formation whatever: (*a*) if poisoned with a small amount of iodo-acetic acid (Lundsgaard) or (*b*) if depleted entirely of carbohydrate, e.g. by the administration of thyroid and insulin. Fatigue and slowing of contraction are probably in the normal muscle due in part to the disappearance of creatine phosphoric acid, and in part to the accumulation of lactic acid.

Fatigue in man.—Fatigue in man, as the result of violent exercise, is mainly a matter of inadequate oxygen supply to the active muscles. Muscles may exert themselves for a short time ten times as actively as their maximum oxygen supply would allow. The oxygen supplied through the circulation cannot keep pace with the demand, phosphagen breakdown and lactic acid production occur, and recovery becomes necessary. In recovery combustion takes place and the energy supplied allows, so to speak, the accumulators to be re-charged. The oxygen necessary for recovery after a bout of exercise is referred to as the "oxygen debt" incurred during the exercise. The oxygen debt may attain considerable amounts—in an athletic subject 15 litres or more—as much as would be required at rest for about an hour. An oxygen debt of 8 litres may be incurred as the result even of running 100 yards at top speed.

Energy and oxygen.—One litre of oxygen used in the combustion of any of the ordinary foodstuffs gives about 5,000 small calories, about 2,100 kilogram metres, about 15,500 foot-pounds. The maximum intake of oxygen in man may, in athletic subjects, be as much as 4·4 litres per minute, which represents about 2 horse power of total energy. Used with 25% efficiency this would yield mechanical work at the rate of about half a horse-power. This represents the greatest output which can be maintained for any considerable time, and each member of the crew of an 8-oared boat has in fact to develop about half a horse-power in propelling the boat. For very short intervals the output of work may be very much greater, but this is achieved by the possibility of incurring an oxygen debt, of so to speak running the accumulators down and re-charging them afterwards.

The requirements of oxygen, and therefore of energy, for any task can be measured, provided we take account of the oxygen used not only during the exercise but in recovery from it. Standard methods are available to measure the oxygen requirements of man, and in this way a scientific study of muscular work, both in sport and industrial processes, is possible. Much important information has thus been obtained as to the factors involved in muscular effort of various types.

Energy losses during muscular work.—The chief loss of energy as the result of muscular work is, of course, that involved in the recovery process after exercise, during which the "accumulators" are being "re-charged." Apart from this, however, we must consider:—

(*a*) The performance of mechanical work, actual foot-pounds stored in some external object.

(*b*) The overcoming of some external frictional resistance, e.g., air or road resistance.

(*c*) The maintenance of body posture necessary in performing the act required. In some forms of work this may be a very important factor and for efficiency should be reduced to the lowest possible dimensions.

(*d*) The overcoming of the internal "viscous" resistance of the muscles themselves, which in very rapid movements may be a comparatively large quantity.

(*e*) The alternate production and destruction of kinetic energy in the moving limbs: in such processes as rapid running much energy is lost in this way.

The optimum speed.—In many forms of muscular exercise or industrial work an optimum speed exists, i.e., a speed at which a given amount of external work can be performed with a minimum expenditure of energy. The existence of this optimum speed depends upon two factors:—

(*a*) The fact that the external work done by a *given* muscular effort (i.e., the contraction of a given number of muscle fibres stimulated at a given rate) diminishes as the speed increases. This is because at a higher speed more kinetic energy is wasted in the limbs and because more work has to be done in overcoming the viscous resistance of the muscles; and

(*b*) On the other hand, if the contractions involved last longer, more energy is required in maintaining them during the interval necessary.

These two factors work in opposite directions and the ratio of work to total energy reaches a maximum value at some particular speed of movement. It is important in the design of tools and of such machines as bicycles to realize that an optimum speed exists. Long experience has often shown the optimum size, shape or gearing to employ, but a realization of the scientific basis of this may be of value in designing new tools and processes and so in rendering industrial effort more efficient.

This brief summary of the important place occupied by energy exchanges in the processes of muscle and nerve has made no reference to the instruments and methods

involved in obtaining the results described. In lecturing, however, to this Section of Physical Medicine, it may not be out of place to conclude by a few references to two of the physical devices which have resulted from, or been used in, investigating the problems of muscle and nerve.

(*A*) In studying the resting heat production of muscle a curious phenomenon observed led finally to the discovery that the delicate thermopile employed for measuring the temperature difference between the muscle and its surroundings was acting as a highly sensitive recorder of vapour pressure. The realization of this allowed one to devise a delicate and accurate method of measuring osmotic pressure, either in living tissues or in small quantities of fluid. The total osmotic pressure of a solution is directly proportional to, and can be calculated from, the depression of vapour pressure which is read by one of these instruments.

The instrument itself is simple in principle. A symmetrical thermopile, with its two sets of junctions in the middle of opposite faces, is placed in a moist chamber in a thermostat. A piece of filter paper, dipped in the solution whose osmotic pressure is required, is placed on one face. Another piece of filter paper, dipped in any standard solution, preferably of about the same osmotic pressure, is placed on the other face. After fifteen to thirty minutes, owing to the difference between the rates of evaporation at the two faces, a difference of temperature is set up between them which can be read with a galvanometer. This difference is proportional to the difference of vapour pressure, i.e., to the difference of osmotic pressure between the two solutions. Hence, that of the experimental solution can at once be determined knowing that of the standard.

This method has been applied to the case of blood and other body fluids. The blood is normally of the same osmotic pressure as the muscle, which in man is about that of 0·93% sodium chloride. In normal people at rest the osmotic pressure of the blood is extremely constant, though for some curious reason it is regularly slightly higher in men than in women. During severe muscular exercise many new molecules and ions are liberated owing to chemical breakdown in the active muscles, and the osmotic pressure of these increases by as much as 20 or 30%. This is rapidly reflected in the osmotic pressure of the blood, which may rise as much as 10% as the result even of one minute of exercise. It may well be that some of the phenomena associated with, and occurring after, severe exertion may be due to the rise of osmotic pressure in the blood, which must act temporarily in dehydrating other organs, e.g., the brain and nervous system.

(*B*) The measurement of heat in nerve has involved instruments of extreme delicacy, as will be realized from the fact that the heat produced by stimulating a nerve for a second corresponds to a rise of temperature of only a few millionths of a degree: which can as a matter of fact be read within a few per cent. The measurement of this heat has involved (*a*) the construction of the finest and most sensitive thermopile possible, and (*b*) the employment of a method of amplifying galvanometer movements. This amplification depends upon the use of a new type of photo-electric cell, which because of its interest and of its many possible forms of usefulness I will shortly describe.

This cell consists of nothing but a copper disc coated with cuprous oxide and sputtered with gold electrically on the surface of the oxide. Contact is made to a galvanometer by leads from the gold film and the copper at the back. When light falls upon the film a current is developed proportional to the total light falling on the cell. No high-tension battery is required and the cell is sufficiently sensitive to give good readings when directly connected to a pointer galvanometer. It can be used to replace visual observation in a colorimeter or an opacimeter. It can be used as a photometer. In the present connection it can be used as an extremely delicate micrometer. Imagine, for example, that we place two such cells (actually a single cell split down the middle) in opposition, one above the other. Let us shine

a strong beam of light on them and adjust it so that approximately equal amounts of light fall on each of the pair. Then if the two cells are moved, even by the smallest amount, the balance is upset, more light now shines on one than on the other, a current is developed and the amount of movement can be read. It is possible in this way, with nothing more than a pair of cells and a sensitive galvanometer, to magnify movements 10,000 times, or in other words to read by 1 mm. on the galvanometer scale a displacement of $0{\cdot}1\ \mu$. This device may be of use to engineers and others concerned with measuring displacements, but it can also be employed to magnify the deflection of a galvanometer. Let us shine a beam of light on to the mirror of a galvanometer and allow it after reflection to fall on a pair of these cells differentially arranged. Adjust the cells so that no current is supplied by them to a second galvanometer. Now when the first galvanometer moves, the spot of light from it changes its position on the two cells, they are thrown out of balance, and produce a current which is recorded by the second galvanometer. In this way it is possible to multiply the movements of the first galvanometer 100 times, and to record them with very little lag by means of the second galvanometer.

This device has been used in recent work on the measurement of nerve heat and has proved very satisfactory. It allows one to go to the absolute limit of galvanometer sensitivity. This limit is set by the fact that it is no use to make the galvanometer so sensitive that it shows Brownian movements of its own. It sounds at first almost incredible, but it is nevertheless a fact, that the moving coil of a galvanometer can be treated as though it were a single large molecule. Give it one third the energy of a gas molecule (for one degree of freedom) and allow this energy to twist it against the torsion of its suspension. The sensitivity now available is so great that the amount of twist applied will cause a perceptible movement of the second galvanometer connected to it *via* the photo-electric cell. I am now using a galvanometer system the sensitivity of which is given by 1 mm. $= 2{\cdot}5 \times 10^{-11}$ amp. The Brownian oscillations are of the order of 10^{-11} amp., i.e., of the order of $0{\cdot}4$ mm. It is impossible by any means to avoid these molecular movements, and it is no good increasing the sensitivity, if by so doing we merely increase also the random disturbances due to unavoidable causes. Just therefore as the microscope employed with visible light is limited by the wave length of the light, so the galvanometer used for recording temperature changes (or any others) is limited by the molecular disturbances that occur in its moving system. These could be avoided by working at a much lower temperature, but even were it possible to imagine all one's apparatus placed in liquid air one could not expect a nerve or a muscle to function under such conditions. It would be no good to have one part of the circuit at a high temperature, another at a low; so long therefore as we have to deal with physiological materials which cannot be frozen, there is an absolute limit to the sensitivity of the galvanometer that can be employed to examine their properties.

Section of Surgery.

[*November* 4, 1931.]

DISCUSSION ON THE TREATMENT OF ACUTE OSTEOMYELITIS.

Mr. Gwynne Williams: In discussing the treatment of acute osteomyelitis, the first difficulty to be met with in assessing the results of differing methods of treatment is the great variety of the disease. This variety combined with the relatively infrequent occurrence of the disease in the ordinary practice of a surgeon, makes it difficult for any one person to come to a satisfactory conclusion.

(1) I shall assume that "acute" osteomyelitis means a sudden illness associated with fever and evidence of inflammation of the bone, the duration of the illness being for days rather than for weeks.

(2) It would be convenient to limit the discussion to cases in which the condition occurs in the bones with a definite medullary cavity.

(3) It would be of advantage to consider only those cases due to the *Staphylococcus aureus*, or at least to consider these separately from the streptococcal group, since it is improbable that the same treatment is likely to be equally successful in both varieties.

It might also be advantageous to consider cases of osteomyelitis in the growing bone separately from those in which the condition occurs in the adult one, but so far as I have seen, the great difference in the adult bone is the slowing of the process, so that such cases do not, for the most part, belong properly to the class of case we are considering.

In assessing the results there should be considered: (1) The immediate mortality; (2) the saving of the limb; (3) the extent of the resulting acute necrosis of the bone; (4) the persistence of suppuration of varying degrees in the bone in after-years.

I have looked over the records of acute primary osteomyelitis of the long bones at University College Hospital during the last 20 years. There were 91 cases, of which only 7 cases were adults; there were 18 deaths. It is not always possible to be sure that they were staphylococcal, but in most cases this fact has been noted. There were ten deaths within from one to four days of the operation. Most of these deaths seem incapable of having been prevented by operative methods; in some cases it might be thought that the shock of the operation and the loss of blood might be factors in influencing the result, but the majority must be regarded as septicæmias, and for the purposes of the present discussion might be omitted.

The next group of deaths, of which there are seven, occur round about the tenth day after the operation, and the usual course of events has been that pus has been found beneath the periosteum, the medullary cavity has been chiselled open and laid bare to the extent to which pus has been visible; the resulting wound has been plugged with gauze and possibly treated with the Carrel-Dakin method. Fever has persisted and the patient has died in about ten days with pre- or post-mortem evidence of pericarditis and other signs of widespread infection. It is clear that a

free opening-up of the bone has not prevented the continued spread of the infection, and it might be argued that the severity of the surgical attack had put the patient at a disadvantage.

This group passes into the next in which, in spite of the appearance of other foci in other bones and joints—and in one case in the pericardium—the patient survives after a long and trying illness. Lastly there are those cases in which the disease remains limited to the bone in which it was first observed.

In order to define the discussion, I suggest that we consider what should be done when, in the absence of obvious septicæmia, we find pus beneath the periosteum, which has been stripped to a greater or less extent from the shaft of the bone.

Twenty-five years ago I was told that if pus could not be seen coming from the bone at the epiphyseal line, the bone should be left alone and not opened up until further evidence for its necessity presented itself, but if pus was seen, the bone was to be opened up to the extent necessary to give free drainage. Following this came the period during which the bone was freely guttered with the idea of producing adequate drainage. Recently the tendency has been towards a more limited attack by means of drilled and trephined holes. Opposed to these methods of drainage there is the method of removal of the diaphysis. Personally I have had little experience of this method, and in spite of its theoretical attraction in removing the whole bony focus I doubt whether it is likely to prove of general application.

At present the question seems to lie between guttering the medulla and drilling the bone, or, as it might be put, between a wide or limited attempt to produce drainage. It is doubtful whether the widest opening up of the bone produces adequate drainage. It is very striking to note, in looking over the temperature charts of these acute cases, that, whatever method of drainage is used, the fever abates very gradually and few of the cases show a fall to normal within a few days, such as one might expect if the drainage had been adequate. The extensive opening up of the bone has failed to prevent a high mortality and the clinical course of the cases in which the patients have survived does not suggest that it succeeds in producing adequate drainage, so that in the early days of an acute primary osteomyelitis less severe measures should be undertaken.

I have recently operated upon a boy, aged 13, admitted after fourteen days' illness with osteomyelitis of both tibiæ and turbid fluid in the left knee-joint. The periosteum had been extensively stripped from the upper two-thirds of the shafts except over a narrow line behind. I did not open the medulla at the original operation but a fortnight later I drilled trial holes in the upper ends; no pus came from the right tibia and a little pus, followed by blood, from the left one. At the end of six weeks there was no bare bone on the right tibia and there were merely small areas with granulations bursting through on the left tibia. The fever continued for six weeks but the general condition was good throughout. This was carrying inadequate drainage of the bone to the limit, and in this case it is so far satisfactory. I do not wish to draw any general conclusion from this case, but it suggests that it may not be necessary to open up the bone if the periosteum has been extensively stripped. It certainly shows that the blood supply to the upper two-thirds of the bone was not greatly damaged by the stripping of the periosteum as it would have been if the bone-marrow had been widely opened up.

In the post-operative treatment every effort must be made to maintain the patient's general resistance. This sounds like a pious aspiration, but something real can be done, and I believe that these patients should be treated in the open air and that they should be kept free from pain by efficient splinting. For this reason, I regard Orr's method of plugging the wound with vaselined gauze and fixing the limb in plaster of Paris as a distinct advance. The patients are free from pain and from the frequent dressing and the anæsthetics which these dressings require. The great disadvantage is the foul smell; this is of less importance if the patient

is in the open air. The other drawback is that the wound and limb are more difficult to get at for inspection; I have not found this a great disadvantage, since if the general condition gives rise to the suspicion that all is not well, it is nearly as easy to remove a plaster-of-Paris bandage as it is a cotton one.

Of the other measures directed towards increasing the general resistance, I should like to hear the opinion of the meeting about blood transfusion.

The saving of the limb in acute osteomyelitis depends to a great extent on the invasion of a neighbouring joint and is as much a problem of the treatment of acute arthritis as of osteomyelitis, and I do not think that I can present you with any evidence of value in this connection. I rather suspect that the problem varies from joint to joint.

The extent to which the more conservative operative measures affect the necrosis of the bone is not easy to assess; my impression is that the less that is done to the bone, the smaller are the sequestra.

Even more difficult is the question as to whether the treatment of the primary attack affects the recurrence of inflammation in the affected bone, and I know of no evidence on which a considered judgment could be formed.

Mr. Eric I. Lloyd: In 1928 the Section of Orthopædics held a discussion on the treatment of acute osteomyelitis,[1] at which I reported some statistics from the Hospital for Sick Children, Great Ormond Street. I have now brought two of the tables up to date. Statistics can be made to prove almost anything, but mine proved nothing unless it was the well-known fact that acute osteomyelitis carries a mortality of between 20% and 60%. All such compilations as these suffer from more than one defect. There is no hard-and-fast line between what is acute and what is subacute, or even chronic. At one end of the scale is the author, who includes such smouldering fires as osteomyelitis of the jaw and at the other is he who almost comes to believe that no case is acute unless the patient dies! It is a question not of dishonesty, but of ignorance. Moreover, statistics like mine represent the results of different operative methods in the hands of different surgeons.

ACUTE OSTEOMYELITIS: H.S.C., 1923-1930.

	Recovered	Died	Total
Ilium	2	1	3
Pubis, ischium	2	0	2
Femur	3	5	8
Tibia	5	2	7
Fibula	1	2	3
Scapula	2	0	2
Rib	1	0	1
Humerus	4	2	6
Radius	3	0	3
Ulna	2	0	2
Spine	1	0	1
Skull	1	0	1
Metacarpal	1	1	2
Total	* 27 (67½%)	13 (32½%)	40

	Recovered	Died	Total
Staphylococcus	16	10 (38½%)	26
Streptococcus	9	1 (10%)	10
Pneumococcus	1	0	1
No culture	0	2	2
Total	26	13	39

* One patient had a lesion in two bones.

1 *Proceedings*, 1928, xxi, 1377 (Sect. Orth., 55).

A friend of mine, in a paper last year upon another subject, remarked that he depended for justification of his method on a statement of the reasoning responsible for it, rather than on the usual table of results. The late Professor Starr might have said the same thing. If Starr's pathology is right his treatment follows, but if it is wrong his method falls with it. The pathology of osteomyelitis has long been considered an important branch of the medical student's knowledge, and "involucrum," "sequestrum" and "cloaca" have, perhaps, been the downfall of many. The pathology taught, however, is that of the dead, and not, as Lord Moynihan would have us learn, that of the living. The truth is that we know more about dead bone than about dying bone.

Everyone believes that osteomyelitis begins its local manifestations at the diaphyseal side of the epiphyseal cartilage, in that part of the shaft which is called the metaphysis. Invasion of the medullary canal often follows, but opinions are still divided as to whether this occurs early or late. You remember how Starr maintained that it occurred late, and hence he condemned all forms of gutter operations, with their extensive devitalization of bone. He advocated drainage of the primary focus only and recommended trephine or drill holes for this purpose.

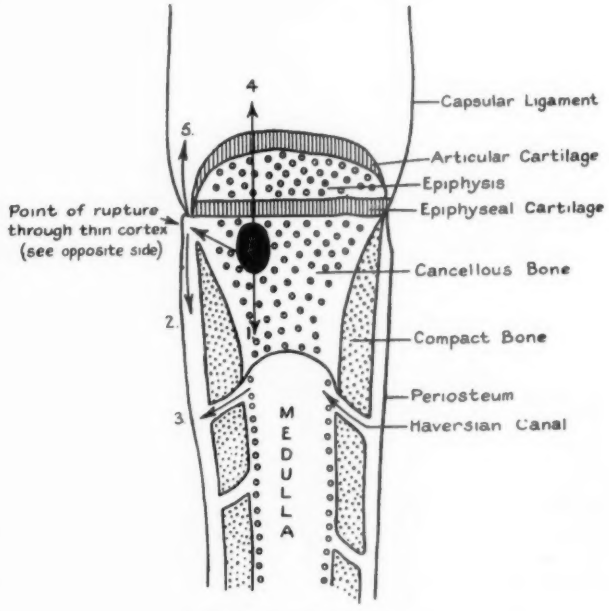

DIAGRAM I. (After Choyce.)

Directions of possible spread from metaphysis.

This diagram from Choyce's "Surgery" shows very well the possible directions of spread, and clearly illustrates the important fact that the compact bone of the shaft is thinnest at a point just below the periosteal attachment to the epiphyseal cartilage. It is here that perforation occurs, and I am inclined to believe that if careful search is made at operation this hole will generally be found at the highest

point of the subperiosteal abscess. Surely it is possible that the occasional success which follows simple incision of the periosteum may be due to an adequate natural drainage of the metaphysis. We cannot, however, rely upon this event or recommend the operation. The proof of Starr's contention that there is always direct communication between the metaphysis and the subperiosteal abscess rests with surgeons and not with pathologists.

Starr went further than this in two directions. He believed that when medullary infection occurs it is not by direct spread, but viâ the Haversian canals in a retrograde direction. He maintained also that, in such an event, the medulla could be safely left to itself if adequate drainage of the metaphysis could be provided.

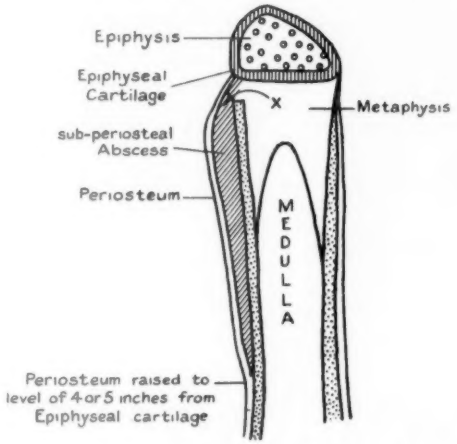

DIAGRAM II.

Osteomyelitis of right fibula: Scheme of operative findings.

The first series of skiagrams (p. 24) illustrates an attempt to combine the ideas of Starr and Orr in dealing with an acute infection of the fibula. The second series (p. 25) shows the good effects of the Winnett Orr method in dealing with a much less acute condition of the radius.

First series (figs. 1 and 2).—Acute osteomyelitis of fibula in a boy aged 12 years. Operation (24.4.31): Three holes drilled into metaphysis. Infecting organism: *Staphylococcus aureus*. Subsequent course.—Plaster eight days later; walked in plaster twenty-three days after operation. Healed in six months; plaster discarded. Afterwards the wound discharged a little and continues to do so from a small sinus, but no further operation has been performed.

Second series (figs. 3 to 6).—Osteomyelitis of radius in a boy aged 2 years and 6 months. Operation was delayed until the formation of a sequestrum which is well seen in fig. 4. The limb was put in plaster at the close of the operation, and the subsequent skiagrams (figs. 5 and 6) show reconstitution of the radial shaft three and five months respectively after operation. The wound healed under the plaster and the scar has remained sound.

Although we may shortly hear criticism of the present-day tendency towards more conservative operative methods, we can scarcely disagree with Mr. Gwynne Williams that "extensive opening of bone has failed to prevent a high mortality."

(*a*) 9.6.31.

(*b*) 9.6.31.

FIG. 1.

(*c*) 24.10.31.

(*d*) 24.10.31.

FIG. 2.

3.3.31.

FIG. 3.

20.5.31.

FIG. 4.

17.8 31.

FIG. 5

30.10.31.

FIG. 6

Mr. W. H. Ogilvie: At the meeting to which Mr. Lloyd has referred, I presented an analysis of some fifty cases of acute osteomyelitis, but as the two facts which emerged from that analysis are well known, I shall not now repeat it. These facts may be briefly stated as follows: That osteomyelitis is a rapidly disappearing disease, and that the death-rate—the only factor to which a numerical value can be given—depends more upon the length of the history and the bone affected than on the method of treatment adopted. If, then, no individual surgeon sees cases of osteomyelitis in sufficient numbers to enable him to give rival methods a trial upon comparable series, and if figures have not much value in pointing the lesson, we are driven to base our arguments and form our conclusions upon matters of surgical principle, a far better method to my way of thinking than any appeal to statistics.

The principles of surgery are eternal, and succeeding epochs differ only in the extent of their elucidation and their manner of interpretation. It is therefore the part of the surgeon to lay stress, in the surgery of osteomyelitis as in that of any other disease, upon the principles that should govern treatment, rather than on the details of some method that may happen to be the fad of the moment. There is a disquieting tendency in British surgery at the present time to follow fashions rather than principles, to accept anything new as *ipso facto* better than that which preceded it. The characteristic responsible for that tendency is an admirable one, an innate national modesty. We are always willing to travel across the Continent to see a master at work, and are often unaware that a compatriot, working within a few miles of our own hospital, is doing the same work very much better.

On this question of osteomyelitis I find myself becoming increasingly insular; that is to say, I am a supporter of the older methods, and of the gutter operation, though I freely admit that recent work has so modified the gutter as to remove from it those disadvantages which had brought it into disrepute in the past.

The two men whose writings have chiefly influenced our attitude on osteomyelitis within recent years and brought it once more into the forefront of surgical interest, are Starr, of Toronto, and Winnett Orr. Their views demand earnest consideration, even though we may not be prepared to accept their conclusions. Starr's opinions, though they have been questioned, have considerably modified our views on the pathology of acute bone disease. That the primary focus is almost invariably in the metaphysis was known to the older writers, but Starr has proved, by observations, both experimental and clinical, which I think we must accept, that though infection spreads rapidly from its point of origin to the surface and thence extends widely under the periosteum, it is arrested for a considerable time by the cancellous tissue of the metaphysis. The medullary cavity is involved late, if at all, and in many instances where the periosteum is stripped off the whole shaft, the central canal is is as yet uninfected. It is not only Starr's pathological evidence, but the success of the method of limited drainage based upon that evidence, which carries conviction. The periosteum and the underlying abscess is laid open to its fullest extent, and the metaphysial area is drained by a series of drill holes, or one or more trephine holes over the area in which pus is found on drilling, but no further.

That excellent primary results are obtained by the Starr method cannot be denied, but it is questionable whether the drainage provided by a series of drill holes is sufficient. In osteomyelitis we have two problems to consider: the immediate one of saving life and limb, and the more distant one of making the cure permanent. No surgeon of ample experience or balanced judgment will claim that any method can promise complete freedom from recurrence in a bone that has once been the seat of osteomyelitis, but where the reparative processes have been effective, such recurrence will be merely minor and local. An abscess in any tissue heals by the falling together of its walls, but the Starr treatment, while it provides immediate drainage of the central abscess in the bone, leaves the process of repair to take place in a rigid cage whose walls cannot fall together. From a careful study of the results of an

English surgeon who has practised the method for many years, I have been impressed by two things: that sequestra have formed subsequently in 60% of his cases, and that his skiagrams seem to show that though at the primary operation the infection appeared to be in the metaphysis only, the whole shaft has subsequently undergone inflammatory changes of minor or major degree, extending from one end to the other. Should the method of limited drainage be widely adopted, future years may see a great many central abscesses and recurrent infections, and possibly late metastases in other bones.

The Winnett Orr method does not, I think, merit the same consideration. I do not understand that it has received any more support in the country of its sponsor than would be accorded to any method that is new and bizarre, nor do I believe that it would have flourished in this country had it arisen here. Its exotic origin is its chief recommendation. But its real beginning was in response to a certain set of conditions. When, in 1916, I was working in a British hospital attached to the Second French Army in the Verdun Sector, the number of wounded daily reaching the group of hospitals centred about Revigny Junction was far greater than could be dealt with by ordinary means. As they were short of dressings and nurses, the French surgeons adopted the plan of treating their compound fractures and joint-wounds by wide débridement, free drainage, copious dressings, and plaster cases. The cases were left in position and the dressings unchanged for six or eight weeks unless the condition of the limb or of the patient urgently demanded further attention. The results were miraculous; many apparently hopeless cases recovered, but, on the other hand, the wounds healed with a maximum of scar tissue, and many knee-joints which might have recovered full movement were permanently ankylosed. This was the origin of the Winnett Orr treatment, and whether Winnett Orr learned the method from France or rediscovered it independently, these are the conditions to which it is especially suited. Where economy in materials and personnel is paramount it is the best method. But where there is a sufficiency of dressings and an adequate nursing staff we should be able to do better.

It is stated that the principles of the Winnett Orr treatment are adequate drainage and complete immobilization. These are the principles of the treatment of osteomyelitis, and we must not allow any attempt to fix a proprietary claim on them. Where the Winnett Orr method fails is in the great and unnecessary amount of fibrous tissue that is formed in the process of healing, and the wide and adherent scar that finally covers the wound. Scar tissue spells loss of function and probable recurrence. Kulowski, writing in the *Journal of Bone and Joint Surgery*, says: "When healing occurred following the Winnett Orr treatment, it was quite permanent." Here speaks enthusiasm rather than discretion. Recurrences will be seen after any method, but minor ones will be less frequent and major ones more easy to deal with if the tissues surrounding the bone are healthy and the skin covering it supple and non-adherent.

Gutter operations have been rightly criticized, because an unnecessary amount of bone is sacrificed, because the subsequent dressings are painful and involve repeated disturbance of the limb, and because the final result is an unhealthy scar attached to bone and liable to ulcerate on the occurrence of any trivial injury. But these drawbacks are accompaniments of the gutter operation—and not necessary accompaniments. Its underlying principle is that the whole of one side of the infected part of the bone is taken away, so that the abscess cavity is laid completely open. The mechanical inducement to further spread is removed, while after the infective process is overcome, its site can be obliterated. The gutter, as it should be practised, has learned restraint from Starr and immobilization from Orr, but has advantages unknown to either.

The bone should be approached by a flap incision. In the tibia, the commonest bone to be attacked, the incision should be about an inch behind the inner border.

For other bones the approaches described by A. K. Henry can hardly be bettered. In any case healthy tissues should be left in contact with the gutter, for they are an essential factor in the repair after the infection has been overcome. The gutter should remove about a third of the circumference of the compact bone as far as pus is found in the metaphysis, not over the area in which the periosteum is raised, for the external pus is no indication of the extent of the internal infection. In many cases a small removal is adequate. No curetting should be done, because emboli might be dislodged thereby, while if the cavity is open such tissue as is necrotic can find ready egress. Drainage is provided by laying Carrell tubes along the surface of the gutter between the overlying tissues and the bone, and the wound is closed by interrupted tissues, loosely tied, between which the tubes emerge. The limb is immobilized in some form of suspension splint, and irrigation is instituted and continued till the pulse and temperature indicate that the infection has been overcome. The dressings need not be changed more often than once every four or six days, for they collect not the foul pus of a plastered leg, but the inoffensive mucoid discharge of an irrigated wound. The dressing is painless since the wound is closed, and does not disturb immobilization since the limb is slung.

This method I have been using for many years in the few cases of osteomyelitis which have come my way. I feel that it is safer than the Starr treatment; I know it to be better than the Winnett Orr, though I still use this and have used it within the last three months for compound fractures involving joints. The method combines the advantages of an open wound as regards freedom of drainage with those of a closed one in regard to the subsequent scar. Discharges are washed away as soon as they are formed, and when the treatment is finished the wide-open space, which can only be bridged by granulations and covered by avascular skin, is avoided. Subsequent operations, through smooth, healthy skin, are very much easier, and their results are likely to be better.

Mr. Max Page: My excuse for speaking is that I opened a discussion on this subject at a meeting of the Association of Surgeons in 1928, and I then advocated the limited operation of periosteal incision. Mr. Boggon had at that time collected some sixty cases, which had occurred at St. Thomas's Hospital in a five years' period, and we found that a large proportion in that group had only had this limited operation carried out. The results, from a statistical point of view, were similar to those presented by most other hospitals, in regard to the immediate mortality, which was 19%. Those figures have been continued by Mr. Sworn, my surgical registrar, who reports that another forty cases have been treated at St. Thomas's in three years by somewhat similar methods. In this last series the general mortality has not altered. But the mortality of the cases treated by periosteal incision is higher than in the early group. My conviction is—and one can only go upon impressions—that periosteal incision is not far wrong, and is better than more elaborate operations, but I think that trephining the diaphysis just below the epiphyseal zone, after Starr's method, is sound. It does little damage, and it opens up a minimum of uninfected tissue, and gives vent to pus, which is present under tension and otherwise may spread down the medulla. I am convinced that extensive operations on the medulla are productive of a greater degree of sequestration and so lead to more trouble afterwards. Mr. Ogilvie says that surgical principles show us the way with regard to technique. I am not sure about that. If you think of the history of the treatment of acute appendicitis you will admit that the surgeon was clear about the principle twenty years ago, and that was to remove an acutely inflamed appendix, and he did so, with a mortality which was anything between 20% and 50%: whereas he does so now with a mortality of only a few per cent. No doubt besides technique other factors have effected this change, but I think operative detail has much to do with the results of the surgical treatment of infection. The surgeon has but limited

power in the matter, and it behoves him to use that power in a timely and precise manner. Speakers this evening have rather overlooked the fact that we are dealing with a hydra-headed affair when we are treating staphylococcal infections. In many cases of osteomyelitis there is a bacteriæmia—staphylococci in the blood—yet many of the patients recover in spite of that. The surgeon does nothing to the staphylococci in the blood, he merely deals with the local infection and prevents active trouble from that. I am sceptical as to how far he can prevent the fulminating cases from going wrong; I do not think he can, however early he gets them. The determining factor is the virulence of the infection and the resistance of the child.

Mr. Gwynne Williams rightly emphasized the importance, in the handling of these cases, of raising the resistance of the patient; the measures which he suggested for doing so are the best we have at present. I agree with him that blood transfusion, as far as I have seen it tried, has not been helpful.

I think the Starr method, on the whole, is the right method of technique for dealing with the situation.

With regard to the Winnett Orr method, as Mr. Ogilvie said, it was surprisingly successful in a certain group of cases and there must be something in it. It is an objectionable method, from the point of view of hospital amenities and impossible to carry out in a closed ward. But its success demonstrates that it is not always necessary to remove pus when it is in a wound; indeed, pus bathing a wound may sometimes be a beneficial thing. I do not know that it is always the right thing to wash away pus as soon as we see it, so long as it is not under tension. We need not go all the way with Winnett Orr, but we can splint the leg and use a pack down the medulla, and not be in a hurry to remove it. Cases I have seen treated in this way have run a benign course.

My remarks have been rather inconclusive, but observed results do not justify a more dogmatic statement.

Mr. A. J. Gardham said he believed that a large amount of the sequestration in ordinary osteomyelitis was not due to the osteomyelitis but to operative interference. No one would deny that sequestration could take place in a bone independently of any form of trauma. One was familiar with such a case in which there had been no operative interference, and yet the whole shaft had sequestrated; but these cases were not as common as those in which the surgeon was troubled for weeks—perhaps for months—with small sequestra, which needed removal at intervals. It was not unreasonable to suppose that where trauma was inflicted in the presence of acute infection, the degree of trauma was as much responsible for the sequestration as was the intensity of the infection. By limiting his interference the surgeon could reasonably hope to limit the subsequent sequestration. He, the speaker, would show skiagrams from two cases which he had chosen out of a fairly large number, as being typical examples.

Case I.—The boy, aged 6 years, was admitted with a three days' history of osteomyelitis. He had a swelling of the thigh, reaching nearly to the hip. He, the speaker, made an incision on the right side of the thigh, and exposed the bone in the situation of a collection of subperiosteal pus, and guttered the bone on the outer side. The skiagram (fig. 1) was taken ten weeks after the operation. The patient had in the meantime developed infection of the knee-joint, which had not been prevented by the gutter operation. There could be seen a large sequestrum, which was subsequently removed, and the position of the sequestrum corresponded with that of the artificial hole which he had made in the bone.

Case II belonged to the period when he had somewhat lost his belief in guttering in the treatment of osteomyelitis. The patient was a child aged 9, the history being almost exactly as in the last case. He (Mr. Gardham) exposed the femur from the inner side, and made a small hole in the popliteal surface. Figure 2 shows the sequestrum, which again corresponded closely with the position in which the hole had been made in the bone.

FIG. 1 (*Mr. Gardham's first case*).

There were two possible explanations. One was the rather beautiful one, which he could not accept, namely, that he had happened to arrange the hole just where the chief point of infection was, having estimated exactly where the sequestrum would be formed. The second and more tenable explanation was that the sequestrum followed on the surgical hole which was made. The evidence in these cases was clear, and he could show a further number of similar appearances. In perhaps 70% of the cases in which there were small sequestra of

FIG. 2 (*Mr. Gardham's second case*).
The sequestrum here lies immediately proximal to the operative opening in the bone, which is shown by an area of increased translucency.

this type, the reason for the sequestrum was the position and extent of the operation, rather than the extent of the infection. If one could prevent a patient dying by making a hole in the bone, though it gave him a sequestrum, one must make the hole. But if guttering or making a hole in the bone had no influence on the course of the disease, it was of greater importance to avoid sequestration. His own present feeling was that opening bone was of no help in improving the prognosis in the acute stage of the disease and was a hindrance to smooth convalescence. The clear indication seemed to be to leave the bone to deal with its

own condition, so avoiding those sequestra not involving the whole shaft, which he believed to be due to operative interference. To those who did not go the whole way with Mr. Gwynne Williams he would say the smallest hole in the right place, i.e., at the epiphysial end of the diaphysis, made with a small trephine, was best.

Case III, the notes of which he had encountered accidentally, gave considerable support to the extreme reactionary view that the bone should be left alone, and not opened. The patient was a boy, aged 9 years, who had a typical history of osteomyelitis of five or six days' duration. A swelling was present about the knee-joint. The swelling was explored,

FIG. 3 (*Mr. Gardham's third case*).

The sequestrum here lies to the inner side of the tibia and corresponds in level and extent with the operative defect in the bone.

and considerable œdema was found, but no pus. Incision of the periosteum did not produce pus, and the bone was not opened. Subsequently the fluid which came from the periosteum yielded *Staphylococcus aureus*. The wound was packed, and the boy was returned to bed. Leucocytosis of high degree was noted, and he, the speaker, advised on the fourth day that the bone should be opened. On removing the packing, pus escaped from the wound. The bone was, however, opened; the temperature went up, and there was a recrudescence of the illness for which the boy was admitted (see chart). The end of the story was that there was a fairly large sequestrum, corresponding exactly in position to the opening made in the bone (fig. 3). He did not doubt that, had the case been left alone, there would have been an

active rarefaction, pus would have made its way out, and the reparative process would have proceeded satisfactorily, with no sequestrum formation.

His view was that in from 50% to 70% of cases of osteomyelitis the sequestration, which worried the surgeon so much, was a direct result of the treatment employed.

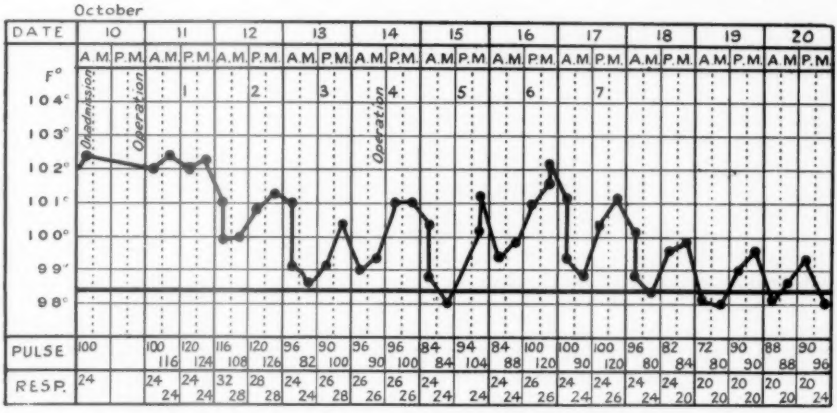

Chart of Case III showing the fall in temperature following simple incision of the periosteum and the recrudescence following opening of the bone.

Mr. C. C. Holman: In considering treatment of acute osteomyelitis we are met by two difficulties. Firstly, the disease is relatively uncommon and few surgeons have records of a large number of cases; my own over a period of ten years total twenty-three. Secondly, the virulence of the disease is extremely variable.

You will agree with me that osteomyelitis is a local manifestation of a systemic infection. It may vary from a fulminating septicæmia which kills in a few days, to a subacute attack which ends in a chronic bone abscess.

My series include two cases of fulminating septicæmia in which death occurred early, and a restricted operation had no apparent influence on the progress of the disease.

At this stage I wish to raise my first point with regard to treatment. The orthodox teaching is, I believe, early diagnosis and immediate operation. Is this wise in very acute cases? Judging by the British Medical Association's discussion last summer the consensus of opinion is against early operation in streptococcal septicæmia and it is well known that in the past many lives were lost by early operation in streptococcal empyema. May not the same principle apply to staphylococcal infection? Might it not be wisest to allow more time for the devolopment of immunity in acute osteomyelitis?

I will now, as briefly as possible, consider the average type of osteomyelitis ranging from the severe to the subacute. My personal notes cover twenty-one of these cases. The bone primarily affected was the tibia in ten cases, the femur in five, the humerus in two, the pelvic bones in two, the ulna in one and the frontal bone in one.

In my experience the majority of patients do not enter hospital until the pus is under the periosteum. Out of the twenty-one cases, in only three was pus still confined to the bone. In four an abscess had formed and burst spontaneously, and in one the abscess had been opened by a doctor before admission. In five cases

admitted with a sinus, including one pelvic case, I operated and removed the necrosed bone. I did this also in the frontal case and in the second pelvic case.

I must now confess that in ten cases in which the pus was under the periosteum, much to the consternation of various house surgeons, I did not open the bone. In such cases I use a tourniquet when possible and make a free incision extending, where the anatomy of the part permits, as far as the pus has tracked. The wound is left open and packed with gauze impregnated with bipp. In the four remaining cases I opened the bone; in three cases because the pus had not reached the surface, and in one, a case of six weeks' duration, in order to deal with a small cavity underlying the subperiosteal abscess. Of these twenty-one patients, only one died, a girl aged 8, who developed a severe suppurative arthritis of the hip-joint secondary to osteomyelitis of the humerus.

The majority of cases treated by simple incision required secondary operations for removal of sequestra of various sizes, but the necessary operation should involve no mortality.

My figures are too small to be of much value. Adequate statistics showing the relation of mortality to method of treatment are difficult to find. The subject is well worth a collective investigation.

In passing I cannot help mentioning some figures given at the discussion by the Section of Orthopædics in 1928.[1] The speaker, after recommending an operation which involved the removal of two-thirds of the circumference of the bone for as far as the abscess seemed to extend, quoted six cases affecting the femur, with five deaths, five affecting the humerus with two deaths, three affecting the fibula with two deaths, four affecting the tibia with one death. It appears as if the death-rate is directly proportionate to the severity of the operation.

In a disease with a high death-rate we must seek the treatment which gives the lowest mortality and not one which gives a speedy recovery in some cases and a speedy death in others. I suggest that it is not essential to open the bone in every case and that extensive interference in the acute stage increases the death-rate.

Mr. John P. Hosford referred to involvement of the epiphysis in acute osteomyelitis of a long bone. He showed a skiagram from a case of osteomyelitis of the upper end of the tibia in a boy aged 10. Four days after the onset of symptoms a gutter had been made in the tibia, but it did not extend quite up to the epiphysis. The skiagram had been taken fourteen days later and showed destruction in the metaphysis in the part between the gutter and the epiphysial line; the same appearance was seen in the adjacent half of the epiphysis. Mr. Hosford commented on the probability of the infection having spread to the epiphysis by way of the vessels which in some cases pass through the epiphysial cartilage. He asked what was the best way of draining the epiphysis when infected: whether from the outside; from the joint which was early involved; or by making a hole through the epiphysial cartilage which, if the infection had spread through by way of a blood-vessel, was macroscopically intact.

Mr. O. L. Addison said that this discussion had filled him with gloom. Were surgeons of to-day going back to the surgery—or perhaps he ought to say, the *want* of surgery—of sixty years ago? which resulted in filling the museums with thousands of specimens of bone trouble. It must be recognized that osteomyelitis was so extraordinarily virulent in many cases that it took its course, no matter what might be done in the way of treatment. He had seen many patients die from twenty-four to forty-eight hours after entering the hospital. He could not see how a trephine hole could be regarded as adequate drainage for anything but the simplest case. He agreed with nearly everything which Mr. Ogilvie had said. In cases in which there were sequestra after gutter operations the reason was that the surgeon

[1] *Proceedings*, 1928, xxi, 1377 (Sect. Orthop., 55).

had not done enough. He himself, so far as he could remember, had never had a sequestrum other than a small flake after doing an adequate operation. Bones, in small children, grew like weeds, and if the surgeon took away sufficient and secured free drainage, there would be no sequestrum formation. The specimens shown this evening of bone recovering from acute osteomyelitis were such as used to be seen in cases which the surgeon had never touched; in each of them were many septic foci left, and there was likely to be a blaze-up of these—and this did happen—at any length of time: he had seen such resuscitation of the disease after fifty or sixty years. The adequate treatment of a really severe and extensive case in the femur was so difficult that one could not look hopefully to a good result. Mr. Lloyd had mentioned this evening eight cases with three recoveries. Of those who did recover, if there was great extension in the femur, i.e., the disease occupying most of the shaft, it could be forecast that they would have trouble for the remainder of their life. In nearly every case in which there was severe involvement of the femoral shaft, the best treatment was amputation. He feared that would sound severe, but it was his view.

Mr. Kenneth Heritage said that, apart from the fulminant septicæmic cases for which little could be done, the whole crux of treatment lay in early diagnosis. Thus any child showing localized exquisite tenderness over a long bone, combined with fever and other evidence of sepsis, should have that bone explored. Diagnosis should not be delayed until either a subperiosteal abscess or gross œdema of the soft parts called for interference, as a negative exploration could do no harm. It was in such cases diagnosed early, whilst the infection was still limited to the metaphysis, that the more recent methods of Starr and Winnett Orr found their chief field of application and most satisfactory results. In these early cases the simpler and less shock-producing technique of Starr had given better results than wide guttering. Under a tourniquet the periosteum was exposed and incised at the point of maximum tenderness. If no pus was found under the periosteum the metaphysis was drilled at intervals, starting near the epiphysial line. A trephine disk was then removed, having for its centre the drill hole from which pus was seen to exude. In such an early case the cavity was then packed with vaseline gauze; the skin incision was brought loosely together and the limb immobilized on a suitable splint. Plaster was useful, probably owing to the absolute rest which was afforded, with freedom from movement and interference. A skiagram of the end-result of such an early case was shown in which the lower end of the femur was affected. Pus was found in the metaphysis only, and *Staphylococcus aureus* was grown. After six weeks the vaseline pack was found to be extruded and lying on a granulating area. No sequestrum resulted. If, however, the pus was found under the periosteum or infiltrating the cellular planes of the limb, complete enclosure in plaster was considered undesirable, as much spreading infection and scar tissue formation might result. Probably the three most important principles of treatment were early diagnosis, metaphysial drainage without opening the medullary cavity, and absolute immobilization.

Mr. G. Vilvandré said that skiagrams depicting sequestra or other conditions were at best merely a gross or coarse presentation of what was happening in the bone. Beyond the abscess or the sequestrum visible in the skiagram there were inflammatory processes going on, or there was infection not revealed, which might be extending an inch or more beyond the margin of the pathological area shown in the picture.

Neither were the skiagrams any criterion or sign of the virulence of the staphylococcal or streptococcal infection in the case. These conditions were to be appraised by clinical signs and examination, and as a result of clinical experience

which the young surgeon might acquire by lengthy study and the watching of a better man than himself.

Mr. Gwynne Williams, in reply to the speaker who asked what one was to do when the epiphysis was involved in reference to the joint, said that he did not know, because he was not aware how one knew when the epiphysis was involved. He would be inclined to wait and see.

Mr. Addison maintained that an extensive operation should be done for the disease, but so far as he (the speaker) could see, the extensive operation had not altered the immediate mortality rate of the disease; he had never maintained that drilling a small hole in the region of the metaphysis would provide adequate drainage; what he had said was that he did not think guttering had proved to be adequate drainage.

Section of Urology.

[*November* 26, 1931.]

Enlarged Prostate.—J. C. AINSWORTH-DAVIS, F.R.C.S.

The specimen is a prostate gland, weighing 136 grm., which I removed in two stages about four years ago from a patient then aged 70 and who, at the present time, has no urinary symptoms.

Apart from its size, there were three points of interest: (1) The considerable elongation and distortion of the posterior urethra, which made cystoscopy absolutely impossible, and which I have only met with in under 2% of my cases. (2) At the first stage, I removed eighteen faceted stones from the bladder, which had in themselves caused no special symptoms leading to their diagnosis before operation. (3) The low degree of renal function as shown by the blood-urea and urea concentration tests.

A fortnight after the operation, the blood-urea was 70 mgm. %, and the urea concentration 0·8% and 1·0% in the second and third hours. For this reason, I sent the patient out with a large Pezzer catheter and permanent belt.

Two months after operation the results of the tests had improved somewhat, the blood-urea being down to 60 mgm. and the urea concentration 1 and 1·2 in the second and third hours.

I did not consider these figures good enough to warrant a prostatectomy, and so postponed operation for another month, when again there was an improvement, the blood-urea being 54 mgm. and the urea concentration 1·4 and 1·8.

The prostatectomy was easy to perform, the prostate itself coming away piecemeal. The enlargement proved on microscopical examination to be innocent in character. It was followed by no complications until the fourteenth day, when the wound was about to heal. An anxious week followed with rigors, rapid pulse and symptoms of renal failure. These cleared up immediately when the wound was dilated and a large Pezzer catheter re-inserted.

I discharged the patient for a second time and allowed the urine to drain suprapubically for six months, when I removed the Pezzer catheter, sewed up the wound and tied a large catheter into the urethra. The wound was dry on the eighth day, the patient left the home in sixteen days, and has remained well ever since.

In connection with this case I should like to know: (1) Whether other urologists have found cystoscopy impossible in certain cases of benign enlargement of the prostate, and (2) what additional measures (apart from fluids and alkalies) can be employed to improve the renal function between the first and second stages of a prostatectomy.

A Piece of Slippery Elm Removed from the Bladder.—J. C. AINSWORTH-DAVIS, F.R.C.S.

The specimen is a piece of slippery elm with phosphatic fragments, removed by instrumental means from the bladder of a woman who was six months pregnant.

When first seen the patient had severe pain and frequency of micturition. Cystoscopy revealed acute cystitis and a phosphatic calculus surrounding a piece of wood which, she admitted on being questioned, she had used to bring about abortion some two months previously and which had been erroneously inserted and lost in the urethra.

I crushed the stone with a cystoscopic lithotrite and evacuated the fragments. As far as possible, I then squashed the piece of slippery elm itself and withdrew it through the urethra with a Young's cystoscopic rongeur.

The patient left hospital seven days later with an undisturbed pregnancy.

I suggest that in cases such as these, instrumental—rather than operative—methods should be given a trial, for the three reasons of safety, shortened convalescence and minimum discomfort to the patient.

Tuberculous Kidney.—HAROLD DODD, Ch.M., F.R.C.S.

In November, 1930, a single woman, aged 23, complained of acutely painful and frequent micturition of a fortnight's duration. She had been perfectly well until June, 1930 (i.e., five months previously) when she vomited repeatedly and had an attack of abdominal pain, worse in the left iliac fossa. She stayed in bed for three

Skiagram showing (*a*) Extensive calcification of abdominal glands, (*b*) Ureteric catheters in position and left hydronephrosis; normal right pyelogram. (*Mr. Harold Dodd's case*).

days and recovered. In July, another attack of similar abdominal pain and frequency of micturition confined her to bed. During August, September and October she convalesced slowly at the seaside, when she felt well again, except that she could only move about slowly, sudden movement causing a return of the pain in the left side. Micturition was again normal except for nocturnal frequency; she was regularly disturbed twice nightly. In October she returned home and was

well for a fortnight, when the pain and frequency returned, and she had had them for three weeks when I saw her first, in November. On no occasion had she noticed blood in her urine.

She was very thin, pale and nervous, and was losing weight. On the left side of her neck was the scar of an operation performed during childhood on tuberculous glands, a mass of which was still palpable.

The abdomen revealed tenderness in the left kidney area, with a poorly-defined swelling which I considered to be the left kidney. Rectally, the left ureter was palpable about the thickness of a little finger. There were no respiratory symptoms suggesting phthisis and X-ray examination of the chest revealed no signs of active tuberculosis. A skiagram of the urinary tract showed unusually extensive chains of calcified abdominal and lumbar glands, but no renal calculus. A catheter specimen of urine showed a few pus cells but no organisms.

The blood-urea was 50 mgm. and urea concentration 1·3 for the first hour and 1·6 for the second hour. Cystoscopy revealed an injected left ureteric orifice discharging pus, and a congested base of the bladder with a small erosion of the mucous membrane near the left ureter. The right ureter appeared to be normal. An injection of indigo-carmine was excreted in seven minutes by the right side, and very faintly, after fifteen minutes, by the left. Tubercle bacilli were found in urine collected from the left ureter but there were no organisms in that from the right side; there were a few leucocytes and red blood-cells. Pyelography showed dilatation of the pelvis of the left kidney, with flattening of the calyces, the appearances suggesting hydronephrosis.

The patient was kept in bed, given ample fluids by mouth and rectum, and bladder sedatives.

The blood-urea, estimated two weeks later, was 44 mgm. (a drop of 6 mgm.), whilst a week later it was the same and the urea concentration poor at 0·8 and 1·9% in the first and second hours respectively. A week later the blood urea further improved to 33 but the urea concentration was further diminished at 0·4% and 1·2%, whilst the frequency and dysuria were no better.

I removed the left kidney and the ureter to the pelvic brim through a lumbar incision. Owing to her poor condition I did not consider it advisable to remove the remainder of the ureter at that time. The kidney showed a well-defined tuberculous abscess 1 in. in diameter, in the lower half, opening into the pelvis. The patient recovered uneventfully but the frequency and the pain were only slightly diminished.

The urea concentration, estimated a month later, was 1·7 and 1·0%, and the blood-urea was 27 mgm., a definite improvement.

Three months after operation the patient had put on a stone and a half in weight, but still had frequency of micturition, hourly during the day and about three times during the night.

I saw her again in September, 1931. She looked very well and her weight had increased by 20 lb. to over 9 st. The frequency was then two-hourly during the day, with occasional shooting pain on the desire to micturate, and twice nocturnally. I thought the glands in the neck were a little larger and there were in addition palpable, deep external iliac masses on both sides. X-ray examination showed a slight increase in the calcification of the abdominal glands. Cystoscopy showed a right ureteric orifice normal in appearance and function. The left ureteric orifice was the centre of a fair-sized acutely inflamed area, to which shaggy, purulent debris adhered in large masses. The urine contained many pus cells and colonies of streptococci were cultured. Urea concentration and blood urea were normal. Through a left paramedian suprapubic incision I removed the remainder of the left ureter, dissecting it out of the wall of the base of the bladder. Externally it was normal in size and appearance. Internally it was dotted with petechial patches of

inflammation. About the ureter were masses of caseous glands, the size of walnuts, lining the pelvis.

The result was dramatic. Within three days the pain and frequency had disappeared, the patient reported more comfort on micturition than she had had for eighteen months, and she had no nocturia. This progress has been maintained—except for a slight return of frequency for forty-eight hours a week after the operation.

The case is interesting on several points: (1) The initial pain only occurred on exercise, suggesting a stone rather than an inflammatory lesion. (2) In spite of careful and prolonged treatment before operation, the poor renal function continued to be very little improved, showing the toxic effect of the bad side on the sound kidney. (3) The remainder of the left ureter from being the thickness of the index finger became apparently normal in eight months but was still inflamed and causing symptoms which were quickly relieved on its removal.

Postscript.—(February, 1932.)—No symptoms whatever.

Nephro-Uretero-Cystectomy for Widespread Papillomatosis. — JOHN EVERIDGE, F.R.C.S.

Patient, male, aged 31, operated upon for perforating gastric ulcer two years and a half ago. At this operation, Dr. Haworth, the surgeon, noted a large fluctuating retroperitoneal mass, and having completed his operation, introduced an exploring syringe into it. Blood-stained fluid was withdrawn and during the next few days the patient had hæmaturia. Some weeks later I was asked to investigate. Chromocystoscopy revealed a large papilloma in the region of the right ureter, and a free escape of well-stained urine from the left ureter. The papilloma was fulgurated. By this time the retroperitoneal swelling had become enormous; it occupied the whole of the right flank and extended beyond the middle line towards the left, it extended down into the pelvis and was even palpable on rectal examination. It had all the characters of a huge hydronephrosis. Lumbar nephrectomy was performed and the hydronephrotic kidney was delivered with considerable difficulty, on account of its vast size. The ureter was as large as the small intestine, and was tightly distended with massed papillomata. It was divided in the neighbourhood of the fourth lumbar vertebra. On examination, the kidney pelvis was found to be crowded with papillomata so much compressed as to appear as a solid mass strongly suggestive, to the naked eye, of carcinoma, but microscopy proved its innocent nature.

A fortnight later uretero-cystectomy was carried out. The right rectus was split and the peritoneum separated up from the bladder, the patient being in the high Trendelenburg position. The ureter, on account of its distended condition, was easily found and traced to the bladder. The posterior aspect of the bladder was carefully exposed and a circular incision made through its coats from without inwards, including a wide area, the site of the papilloma which had previously been seen in the bladder cystoscopically. The bladder was then opened anteriorly and the posterior wound in it sutured from within, leaving, however, sufficient space for transvesical extraperitoneal drainage. The upper end of the ureter was carefully traced to the point where it had been ligatured at the previous operation and the whole length of the ureter, together with the section of the bladder, was removed *en masse*. Healing was rapid and uninterrupted.

Cystoscopy was carried out subsequently at intervals but no recurrence was observed. The general condition of the patient has remained good ever since the operation.

There are two points of interest in this case: (1) That on original section the growth presented all the naked-eye appearances of carcinoma, but the microscope proved to be innocent.

(2) Although we were obviously dealing with a very active growth, the removal of its primary source completely aborted recurrences. I am inclined to think that the bladder has a higher resistance to papillomata originating in the kidney than to those beginning in the bladder itself.

Angioma of Epididymis.—JOHN P. HOSFORD, M.S.

W. L., male, aged 15, in September, 1926, had a blow on the right testicle; this was followed by a shooting pain which soon subsided completely. A month later there was a sudden severe pain in the right testicle and the patient noticed considerable swelling of it. The pain subsided after a few days' rest in bed, but the swelling, after diminishing somewhat in size, remained.

On examination, the testicle was found to be enlarged to twice its normal size, was firm in consistency and not tender. The epididymis could not be felt.

In December, 1926, orchidectomy was performed.

Specimen.—The tunica vaginalis is normal. The body of the testicle appears to be normal, apart from being somewhat compressed by a mass a little larger than itself. This mass, macroscopically, looks like a cavernous angioma and microscopically it consists of blood spaces of varying sizes; no elements suggesting a teratomatous origin can be seen. No epididymis could be found on the fresh specimen and this cavernous angioma appears to take its place.

The patient is alive and well, five years after the operation.

Foreign Bodies found in the Bladder.—A. CLIFFORD MORSON, F.R.C.S.

Mr. Clifford Morson showed a number of specimens of vesical calculi to illustrate the result of the neglect of one of the first principles of bladder surgery, namely, that no substance which cannot be absorbed by the tissue fluids should be permanently retained within the cavity or the wall of the bladder.

He demonstrated the following:—

(1) Stones with nuclei of silkworm gut which had been used to sew up the bladder wall in a case of traumatic structure.

(2) A calculus formed around a silk suture. The suture had been used to close a hole in the bladder wall made during an operation for Cæsarean section

(3) Calculous deposits around radon seeds inserted into the bladder wall for treatment of a growth.

(4) A stone with a nucleus of hair, probably pushed into a female bladder by means of a catheter.

(5) A stone formed around a piece of slippery elm. The latter had been inserted by a woman into her bladder to procure abortion. She was pregnant for the thirteenth time. On realizing her mistake, she pushed another piece of the bark into the cervix, and produced the result she desired.

Carcinoma of the Renal Pelvis.—E. W. RICHES, M.S.

Specimen of right kidney from a woman aged 75, who complained of recurrent attacks of painless hæmaturia, each lasting about three days, at weekly periods.

Physical examination negative. Urine contained blood, otherwise was normal. Skiagram, negative. Cystoscopy showed blood coming from the right orifice only. Excretion urogram showed a normal left kidney, and a blurred indistinct outline on the right. Pyelography showed a filling defect in the right kidney.

Right nephrectomy August, 1931. Recovery.

The specimen shows a nodular carcinoma arising in the renal pelvis, infiltrating the kidney, but not reaching the cortex.

Microscopical examination.—Non-keratinizing squamous-celled carcinoma. This is one of the rarer types of malignant new growth of the kidney.

Specimens from Two Cases of Total Cystectomy.—BERNARD WARD, F.R.C.S.

Case I.—Patient, aged 57, suffering from hæmaturia. On cystoscopy the bladder was found to be perfectly healthy, but blood was seen spurting freely from the left ureter. My colleague explored the kidney and found a large papilloma in the pelvis, and therefore he performed nephrectomy. Seven years later, the patient was referred direct to me on account of hæmaturia extending over several months. Cystoscopy then revealed a bladder which appeared to be filled with growth, so much so that any exact localization was impossible, but it seemed certain that this must be an instance of implantation of a papilloma into the ureter, with secondary spread to the bladder. It was so extensive that only total cystectomy and removal of the remaining portion of the left ureter held out any hope of cure. Transplantation of the right ureter by Coffey's technique was therefore carried out, the catheter being brought out through the anus and drained into a bottle. The subsequent progress was uneventful, without rise of temperature beyond that normal after an operation of this extent. The urine draining into the bottle remained sterile, and repeated urea concentration tests showed that the secretion of the kidney remained normal. The catheter came away on the ninth day, having drained perfectly throughout.

Total cystectomy was performed one month later, the seminal vesicles being dissected off the base and the prostate tied with a stout silk ligature and cut through below the neck of the bladder. Unfortunately, during the operation, the left ureter, which it had been intended to dissect out, was either torn or cut through and the end could not be found, and it was thought wise not to open the peritoneum and search for it—an error of judgment which eventually cost the patient his life. The operation was carried out through a vertical incision and entirely extraperitoneally, the peritoneum being easily dissected off the bladder. There was no shock after the operation, and the patient made a perfectly good recovery. About four months later the lower part of the wound broke down and remained open until the silk ligature which had been tied round the prostate was discharged. It then rapidly healed. After the cystectomy the patient remained well in every way, doing his normal work, for nearly five years; during this time repeated blood-urea tests were carried out, and the blood-urea was always between 40 and 50 mgm. %. He then began to suffer severe pain in the left iliac region and back, referred down the left leg, and later a solid œdema of this leg developed. He then went rapidly downhill, and died in March, 1931.

Post mortem, an extensive solid growth was seen along the line of the lower two-thirds of the left ureter, invading the psoas muscle, the lumbar plexus and the left iliac vein. Microscopically, it was a papilliferous carcinoma, and there were secondary deposits in both lungs, liver, spleen and opposite kidney. There can be no question that this growth had arisen in the left ureter. The right kidney was a third larger than normal, but there was no dilatation of the pelvis or of the ureter. The opening of the ureter into the bowel formed a perfect valve, and distention of the bowel with water under pressure proved that there was no regurgitation up the ureter. On microscopical examination the kidney was reported by the pathologist as normal, except for several small secondary nodules of growth.

Case II.—This patient, aged 43, had a suprapubic operation in 1926, at another hospital, for papilloma of the bladder. The bladder was opened again in 1928 at the same hospital on account of recurrence of the growth. During 1929 he was treated by fulguration through the cystoscope on several occasions. He was first seen by me in April, 1931, five years after the first operation. He then complained of almost continuous hæmaturia, with the passage of clots and intense strangury. It was almost impossible to see anything with the cystoscope, as the bladder was so

full of growth. The blood-urea was 67 mgm. %. Nothing short of total cystectomy appeared to give any chance of curing the patient.

May 17, 1931.—Simultaneous transplantation of both ureters into the rectum by Coffey's method. Both ureters were dilated, and could be seen as semi-transparent cords beneath the peritoneum. Two No. 7 Kidd's bulbous ureter catheters were tied in the ureters and brought out through the anus. That in the left ureter drained uninterruptedly; the one in the right ureter became blocked on several occasions, but was freed by passing the stylet, and by gentle washing out. The urine from both sides remained sterile, and excretion was good. Recovery after the operation was so uneventful that three weeks later total cystectomy was carried out. In this case a transverse incision was used, with partial division of the recti muscles, which gave a far better exposure than the vertical incision in the previous case. The whole operation was carried out extraperitoneally. The seminal vesicles were dissected off the back of the bladder; the prostate was exposed back and front, until it formed a pedicle to the bladder, and was then deliberately divided, a little at a time, from before backwards, just below the neck of the bladder, bleeding points being picked up as they were divided. A few stitches then closed the prostatic urethra. There was no shock following the operation, and the wound healed without incident. Three weeks after this operation the blood-urea was 44 mgm. %, and has since then varied between 40 and 50; a week ago it was 45. The patient has returned to work and is in perfect health. Intravenous pyelograms taken a few days ago, although not too good, appear to show some slight dilatation of the pelvis of both kidneys, but probably not more than was present before operation.

These two cases have proved that total cystectomy is by no means a difficult operation, nor is it one dangerous to life. Transplantation of the ureters, on the other hand, is an operation of extreme delicacy and some difficulty, this being largely due to the fact that it has to be carried out deep down in the pelvis. At the same time, these cases prove that it can be performed successfully, and that Coffey's technique is a very great advance on anything that has gone before. This I have proved to my own satisfaction by several other successful cases, and I am extremely hopeful that we have here a method which further experience will prove to have eliminated many of the dangers previously associated with this operation. If so, the surgery of carcinoma of the bladder and of the prostate will have entered on a new era.

Mr. CYRIL A. R. NITCH, M.S., showed the following specimens.

(1) Focal Nephritis Simulating Hæmangeioma.

Male, aged 21. Previously healthy. Sudden acute pain in right loin and profuse hæmaturia. Blood-pressure 140/85.

Cystoscopy.—Blood pouring from right ureteric orifice. At operation several raised dark-red subcapsular patches resembling hæmangiomata were visible on the surface of the kidney. Nephrectomy.

Microscopical examination showed slight general chronic interstitial nephritis with many advanced subcapsular foci giving rise to raised hæmorrhagic patches resembling hæmangeioma.

Progress.—Eight months later: General condition satisfactory and urine free from albumin and casts.

(2) Chronic Priapism due to Carcinoma of Corpora Cavernosa.

Male, aged 59. Painful priapism for five weeks. No urinary symptoms. No constitutional cause. Both corpora cavernosa near pubis were hard and crura were firm. Anterior urethra and prostate normal.

Biopsy.—Carcinoma of corpora resembling hypernephroma.

Operation.—Complete amputation of penis. Extensive growth invading whole length of crura.

Death from dissemination five months after operation.

(3) **Two Cases of Total Cystectomy.**

(I) Female, aged 44. Papilliferous carcinoma on base of bladder permeating trigone.

Preliminary transplantation of both ureters into rectum by modified Coffey technique, followed by total cystectomy three weeks later.

A section taken through trigone and internal meatus was permeated with carcinoma cells.

Progress.—One year later the patient was reported as being quite well and able to retain urine for from five to eight hours.

(II) Female, aged 53. Nephrectomy for papilliferous carcinoma and subsequent ureterectomy for papillomata in 1929-30. (Reported to Section, March, 1930.)

As benign papillomata were recurring in the bladder at an alarming rate, total cystectomy, preceded by transplantation of the left ureter into the rectum, was performed, February, 1931.

Present condition.—Patient is leading her usual life but looks ill. Can retain urine for as long as eight hours. Recent occasional blood-stained sputum due to metastatic growth at base of right lung.

Prostatic Pouch associated with Congenital Spinal Deformity.—H. P. WINSBURY-WHITE, F.R.C.S.

Patient, male, aged 42, complained of incontinence of urine for six months. He suffered from considerable frequency of micturition (every hour during the day, and four times during the night). He was a somewhat dwarfed individual owing to a marked scoliosis.

On examination I found a discharging sinus from the right epididymis which was enlarged, hard and adherent; the left was also somewhat fibrosed. He micturated slowly and with some difficulty. The urine was turbid with pus in both glasses, and yielded *B. coli* on culture. There was no obstruction to the passage of a catheter, and the bladder contained 11 oz. of residual urine.

On making a rectal examination I found uniform thickening in the prostatic region. Cystoscopy showed a trabeculated bladder with a good deal of localized cystitis. The intravenous injection of 0·4% indigo-carmine resulted in the dye being ejected from the right ureteric orifice in twelve minutes, in poor concentration, while it was not seen at all from the left after an observation of fifteen minutes. Posterior urethroscopy revealed the orifice of the pouch on the floor of the prostatic urethra. A plain skiagram showed that both the eleventh and twelfth dorsal vertebræ were wedge-shaped, instead of cylindrical, and that this condition had given rise to a marked lateral curvature of the lumbar spine towards the right side. On inspecting the back one found a small dimple in the spine just above the tip of the coccyx. An intravenous pyelogram revealed a certain amount of dilatation of the right ureter and also the left renal pelvis. A cystogram showed widespread small irregularities of the bladder outline, indicating trabeculation.

I carried out a further investigation of the prostatic pouch by passing into its orifice a ureteric catheter and then injecting opaque medium. The illustration shows the extent of the pouch clearly outlined in the antero-posterior position. It is seen to occupy the whole area between the inner margins of the obturator foramina extending downwards as low as their inferior margin and very nearly to the top of the symphysis pubis. As the bladder is also filled with opaque medium it is easy to see that the pouch is separated by a considerable interval from the vesical cavity. A skiagram taken under the same conditions, but with the patient in the oblique

lateral position, shows how much within the pelvis the pouch is situated, as indicated by the considerable distance to which it rises above the bulbous urethra.

I approached the sac through a perineal incision and was able to excise the bulk of it, but failed to remove the highest portion which extended upwards behind the triangular ligament. The resection of the sac was laborious, for the reason that it had replaced the prostate, and that there were inflammatory adhesions binding it to its surroundings. Moreover the fact that it extended upwards behind the triangular

A cystogram with a prostatic pouch below. The opaque medium was injected into the latter after a ureteric catheter had been passed into its orifice. (*Mr. Winsbury-White's case.*)

ligament, where it was out of sight, made it impossible to resect this portion of the sac. It was therefore packed with gauze in order to promote the formation of granulation tissue. Following the operation the patient had a perineal fistula for some weeks, but this finally closed. Ultimately posterior urethroscopy showed no evidence of the orifice of the pouch, and the residual urine was found to be reduced to 4 oz.

Leucoplakia of the Bladder.—H. P. WINSBURY-WHITE, F.R.C.S.

The patient was a married man aged 41, with three children. I first saw him in February, 1930, when he complained of frequent micturition with pain at the end of the act. The history was that in 1913 he was admitted to St. Thomas's Hospital suffering from hæmaturia. His bladder was opened and a small papilloma was

excised. The growth was reported to be an inflammatory mass. He was readmitted in 1921 when cystoscopy showed a bright red mucosa, the bladder being in a state of considerable contraction, as it only held 4 oz. Flakes of lymph about the mucosa were noted. The patient had a considerable degree of phosphaturia at the time.

He said that since 1914 he had seen sediment in his urine and had been troubled with frequency of micturition and urgency and discomfort at the end of the act. He had for many years up to the time I first saw him, carried out his occupation of a labourer. He denied ever having had syphilis or gonorrhœa.

The condition which I found on examination was as follows: The patient was of a spare build, but otherwise looked well. Both epididymes were somewhat thickened but not adherent to the testes. There was no evidence of urethral discharge. On rectal examination nothing abnormal could be noted. The urine was turbid and contained débris, which was more marked in the second than in the first glass. A detailed report on the urine showed the presence of amorphous and triple phosphate and a moderate number of pus cells and bladder débris entangled in mucus on microscopical examination, while a strong growth of the *B. coli* resulted from cultivation. Investigations for tubercle bacilli were carried out on a number of occasions without revealing the presence of these organisms.

An endeavour to cystoscope the patient was unsatisfactory, as on attempting to fill the bladder, the fluid at once returned outside the cystoscope, and no more than 1 oz. was retained. Under these conditions the only information obtained was that the vesical mucosa was pale and covered with masses of mucoid material. Posterior urethroscopy showed the roof of the posterior urethra to have the same pallor as the bladder.

A plain radiographic examination of the urinary tract showed no evidence of calculus. Further radiograms taken after the intravenous injection of uroselectan, showed no further abnormality in outline of the kidneys or ureters than a very slight degree of dilatation on the right side, but the poor density of the shadows obtained indicated reduced renal function on both sides. Blood examination showed the Wassermann reaction negative, Vernes 0, and resorcin test with an optic density of 95.

I decided to investigate further by opening the bladder suprapubically. On doing so I found a thin-walled organ which had all the appearance of a normal capacity, but presented a most remarkable appearance. The mucous membrane was uniformly bluish-grey in colour, except on the trigone where ulceration was present. At the margins of the incised vesical mucosa the thickening of the vesical epithelium was apparent. The ulcerated area roughly occupied the trigone, with several finger-like processes extending beyond these limits; one of them reached towards and beyond the left ureteric orifice. There was no undermining of the epithelium bordering the ulcer. On the contrary the edges were somewhat rounded from œdema. The thickened epithelium in the vicinity of the internal urinary meatus was somewhat corrugated, doubtless from the contraction of the sphincter.

A striking feature of the mucous membrane was the way the whole surface except the trigone became and remained completely dry after swabbing. Scattered particles of non-adherent phosphatic grit were removed by the same process. The ultimate result was a dry glistening bluish-grey appearance, suggesting the new skin formed over a somewhat recent scar.

An attempt was made to catheterize the ureters during this investigation, but the difficult approach to the left orifice made it impossible on this side, while the opposite orifice was so obscured by the thickened epithelium that it could not be found.

After removing portions of tissue for microscopical examination from the margin of the ulcer and from the bladder wall at the site of the vesical incision, the wound was closed round a tube draining the bladder. The microscopic sections both showed that the epithelial lining of the bladder was squamous in type, with keratinization of

the superficial layers, a well-marked stratum granulosum, and well-developed and numerous tongues of epithelium projecting deeply into the underlying connective tissue. In places masses of epithelium, isolated from the overlying layer, indicate the marked degree of epithelial hyperplasia. The penetration of these cell masses could not be found so deeply as the muscular coat, and their isolation from the superficial epithelium is readily explained by the manner of cutting the section with the knife. No area could be identified which would justify the diagnosis of malignancy, but the evidence of marked epithelial activity indicates the tendency towards malignant transformation.

Up to twelve weeks after the operation the suprapubic fistula had failed to close completely. In consultation with my colleague, Mr. Stanford Cade, it was decided to implant radium under the ulcerated area. Mr. Cade undertook this and I had the benefit of assisting him. I was able to note that the condition of the ulcer on the trigone was not appreciably altered from that which existed at the previous cystotomy. Four 1·3-mgm. radium needles were inserted beneath the ulcerated surface and left in position for seven days. The suprapubic fistula was soundly closed in seven weeks, and the patient was discharged from hospital and returned to his work.

Before he left hospital cystoscopy showed the same appearance of the bladder as before, but with regard to the trigone although some œdema was noted no ulceration could now be seen.

Nine months later the patient reported for a further examination. After discharge from hospital he had resumed his manual work, and was still in employment. Although he was a little thin he had the appearance of fairly good health. On this occasion it was found that the symptoms were practically the same as before I first opened the bladder. It was noted, however, that there was a slight mucopurulent urethral discharge. This apparently had been present for several months. No gonococci were found in subsequent bacteriological examination.

In accounting for the discharge I remembered that the leucoplakia had been observed in the posterior urethra on urethroscopy. The urine was still turbid, and contained débris. An attempt at cystoscopy was no more successful than on previous occasions, the irrigating fluid being ejected at once outside of the cystoscope.

Various theories have been advanced with regard to the ætiology of this condition, for example: (1) Misplaced embryonal rests of ectoderm. (2) Metaplasia in which the cornification of the epithelium is said to be due to irritation which in its turn results from infection. The difficulty of assessing the value of this theory is to know whether the irritation precedes or follows the change in the epithelium. (3) The most recent theory put forward is that the condition is a deficiency disease. There is both clinical and experimental evidence that epithelial hyperplasia arises as a result of this.

The prognosis in a case such as this seems extremely bad, as no form of treatment seems to influence the condition, while the ultimate prospect of malignancy is always present.

Migration of an Hour-glass Renal Calculus.—H. P. WINSBURY-WHITE, F.R.C.S.

The patient was a man, aged 52, who, three years before I saw him, had had an attack of left-sided renal colic. A skiagram taken at this time showed a small rounded stone in the position of the middle calyces of the left kidney. One year later another radiogram indicated that the stone was in the same position, but that it had now assumed an hour-glass shape. Two years later another radiogram showed definitely that the stone was lying in a position corresponding to that of the pelvo-ureteric junction. An intravenous pyelogram confirmed the fact that the stone was

in this position, and was causing a moderate degree of renal dilatation. I cut down on the kidney and found the calculus tightly impacted; and if I had not seen the skiagram showing the stone in the renal calyces I would have considered that it owed its shape to its impaction at the pelvo-ureteric junction. The patient made a good recovery from the operation.

The stone on removal was half an inch in length. It is a point of great interest that a stone which assumes such a characteristic shape as a result of being moulded by its surroundings in the kidney, could be dislodged and pass on to another situation. Knowing that this can occur, one might almost have hoped that there was still a chance for this calculus to find its way down the ureter, but the degree of impaction which revealed itself while I was handling the kidney during the operation made it quite clear that this was not possible.

Horseshoe Kidney.—T. P. DUNHILL, C.M.G., M.D.

W. D., male, aged 24, enjoyed good health until June, 1930, when a sudden attack of pain occurred, beginning in the hypogastrium and radiating to the right lumbar region. At the end of a week he entered a hospital. X-ray examination did not reveal anything abnormal. An appendix abscess was suspected, and an operation performed. The appendix was normal, but a swelling was palpated in the kidney region. The abdomen was closed.

Patient was admitted to St. Bartholomew's Hospital fourteen days later. A mass was then palpable in the right side of the abdomen. The urine contained albumin, and a few pus cells. The blood-urea was 50 mgm. %. Solution of uroselectan (40 grm.) was given intravenously. On X-ray examination the renal pelvis on the left side was well outlined. No shadow was seen on the right side.

Cystoscopy was performed, and intravenous injection of indigo-carmine given. The dye appeared from the left ureter in five minutes; none appeared on the right side.

Pyelography showed slight dilatation of the left renal pelvis. On the right side a very large shadow was shown. Diagnosis of right hydronephrosis was made.

I performed nephrectomy in August, 1930. The kidney was large and cystic, and a large hydronephrosis was present. The lower pole of the kidney was followed across the vertebral column. It was then realized that a horseshoe kidney was present, and with the patient's consent the condition was dealt with by operation on August 29, 1930, the kidney being divided in the mid-line through an isthmus of renal tissue 2 in. broad and 1½ thick. Bleeding was controlled, drainage provided for, and the incision closed.

Convalescence was uneventful, and the patient is in normal health. Examination of the half removed showed that the pelvis was enormously dilated and contained pus. The right half of the horseshoe kidney had been practically destroyed.

Section of Neurology.

[*November* 19, 1931.]

DISCUSSION ON THE INNERVATION OF THE BLADDER.

Dr. P. C. Cloake: I have tried to discover whether recent anatomical and physiological research on the bladder has brought us any nearer to an understanding of disorders of vesical function as seen in clinical neurology.

I have naturally had to adopt those views of vesical physiology that seem to be best adapted to the facts as we know them at present, though a survey of the results of many workers in this field reveals differences and incompatibilities.

My task has been difficult, not merely because of the limitations of my own knowledge, or of the imperfect agreement of the conclusions of experimental physiologists amongst themselves and with those of clinical medicine, but because of the crudity with which vesical symptoms are commonly recorded in writings on neurology. Terms such as retention, incontinence, or dribbling, usually without qualification, are often the only records felt by the writer to be necessary.

Needless to say such records are valueless to the student of vesical neuropathology.

One becomes convinced that hardly any records exist to-day which are of any use to him, and that neurological case-records will have to include an intimate study of the bladder, at least as thorough and detailed as that of the eye, before we shall be able to understand vesical changes which result from nervous lesions.

This predicates a close association between the urologist with his special knowledge and instruments of precision, and the neurologist with his. This paper will have achieved more than it deserves if it convinces you of the need for such coöperation.

The process of normal micturition includes a filling and an emptying phase. During the former the bladder distends progressively, accommodating its size to its contents through adjustment of its postural tonus, though the intravesical pressure rises gradually to 18 centimetres of water. During the filling phase the bladder is under the predominant influence of the sympathetic part of the autonomic nervous system, which, while adjusting relaxation of its walls, reinforces the contraction of the internal vesical sphincter. I say, "reinforces," because the internal sphincter is well contracted, during filling, after excision of the sympathetic nervous supply [1], this contracture depending upon a parasympathetic reflex. When the intravesical pressure has risen to some 18 centimetres of water rhythmical contractions of the bladder wall become stronger and the pressure is raised greatly during the contraction. Afferent impulses, travelling chiefly by the sacral autonomic (parasympathetic) fibres, reach and pass upwards in the central nervous system to the brain where they result in a consciousness of bladder fullness and a desire to micturate [2]. In the normal individual after babyhood the internal sphincter of the bladder is only opened in response to a stimulus from the brain, whether desire to micturate is present or not, but in infancy the rise in pressure which follows upon the rhythmical contraction of the bladder wall appears to initiate a parasympathetic reflex which relaxes the internal sphincter and increases the contraction of the detrusor muscle, so emptying the bladder.

This reflex is brought gradually under the control of higher centres in the

brain after the first year of life or earlier, and never appears again as an independent mechanism unless the connections of the brain, and the centre for this parasympathetic reflex are completely severed, in which case automatic reflex micturition may again be manifested.

Voluntary micturition.—Even when no sensation of fullness of the bladder is present, micturition can, of course, be performed perfectly. It may be a matter of personal observation that contrary to what has been commonly alleged [3] micturition under these conditions involves no contraction of the abdominal musculature or diaphragm to increase intra-abdominal and thence intravesical pressure; nor does it involve any contraction of the levator ani muscle [4], any of which voluntary contractions could easily be appreciated if performed. I do not say that such increase of intra-abdominal pressure may not be effected as an adjuvant mechanism, but that it is not a necessary part of micturition, whether desire to micturate is present or not. Hence micturition is not started by a forcing of the internal sphincter by pressure exerted indirectly upon the bladder by voluntary muscles (Goltz theory).

What is necessary for voluntary micturition, whether desire is present or not, is an appropriate environmental setting and a mental action which we call volitional. Whether a sensation of bladder fullness has been present before or not, a strong erethistic bladder sensation is now experienced, urine begins to flow and the bladder is emptied. This sensation I believe to be due to contraction of the detrusor musculature of the bladder; it lessens when the flow starts, but is felt to a less degree throughout micturition and is greatly intensified if the flow is suddenly arrested voluntarily or otherwise.

Physiologists have found repugnant the conception of an autonomic reflex directly under voluntary control. It is apparent, however, that though in a sense voluntary, micturition differs fundamentally from the willed activity of the skeletal muscles. For example, trifling distractions may prevent the act altogether, in spite of strong voluntary effort in contracting the abdominal muscles and in spite of definite desire to micturate.

Voluntary micturition belongs rather to the realm of conditioned reflexes where we have other examples of reflexes belonging to the autonomic system brought gradually under the influence of psychic stimuli, so that by psychic factors alone they may be effected or inhibited, under appropriate environmental conditions.

As all micturition in man after the age of two or three years is voluntary in this sense, the lower bladder centres never normally act "on their own," and this fact may help to an understanding of the vagaries of bladder disorder, when its significance is fully realized.

When one turns to voluntary inhibition of micturition while the process is actually in being—a voluntary cessation of micturition—I think there can be no question that the action is a willed voluntary action in the literal sense, and probably effected through the external sphincter. I cannot agree with Learmonth's statement that sudden voluntary cessation of micturition leads to no sensation of the bladder trying to overcome an obstruction at its outlet. On the contrary, I should have said that there was the strongest momentary sensation of that kind, the same sensation that I have said always precedes micturition and that I have regarded as due to contraction of the detrusor muscle. It is true that this feeling is transient and that the bladder rapidly adjusts itself to its contents. Further evidence that the external sphincter is contracted to arrest the urinary stream is afforded by the sudden increase in the force of the stream that immediately precedes its cessation and which indicates firm contraction upon the urethral channel.

Effects on micturition of nervous lesions.—(1) *Disease of the spinal cord.*

We do not know accurately what paths in the central nervous system are followed by impulses from the brain which control bladder activity, nor those which convey afferent impulses from the bladder.

It appears certain that the pyramidal tracts do not subserve efferent bladder impulses, for bladder function is not impaired in proportion to the degree of loss of voluntary movement in the lower limbs.

Yet in focal diseases of the spinal cord, if both crossed pyramidal tracts are affected, voluntary control over micturition is frequently disordered also, and it is probable that the paths for control of micturition lie close to the crossed pyramidal tracts in man; a conclusion also reached by Stewart in his experiments on animals.

In slight and progressive focal disease in the spinal cord at any level, if these descending tracts are affected, the earliest symptoms of bladder disorder are defective power of initiation of voluntary micturition and defective power of inhibiting reflex micturition.

The matter is not quite as simple as that, for sometimes there is an inability to micturate even when strong desire to do so is felt, a condition in which one would expect reflex micturition to take place readily. In a case of disseminated sclerosis in which I have recently observed this phenomenon, there is also impotence and it is possible that there is a lesion interfering with the micturition reflex itself as well as the descending spinal path.

If the sensory ascending paths in the cord are damaged, there is imperfect or absent appreciation of bladder fullness. If reflex micturition occurs, as is likely, it may do so with brief or no warning or may be wholly unconscious. A similar disturbance is seen in some cases of tabes. As the lesion progresses the difficulty in micturition increases and usually an increasing retention results, with passive incontinence from overflow. It is remarkable that severe lesions of the cord, of slow development, should not always lead ultimately to periodic reflex micturition as the micturition reflex is cut off from higher control, but this is not the case.

Although there is much evidence both in experimental animals and in man to show that "the spontaneous discharge of urine . . . is a local act which is entirely independent of the nerves which unite the organ (bladder) with the central nervous system" (Elliott) [5], there is also ample evidence that an important co-ordinating centre exists in the sacral segments of the spinal cord. Focal damage in this region produces a different picture from that seen in lesions higher in the cord.

When the sacral segments are the site of focal lesions, retention of urine commonly results, as if the bladder were unable to empty itself without stimuli arriving by the parasympathetic path. Neglected retention would mean, as usual, overflow incontinence. In some cases micturition is possible but may be weak in force, or the bladder may be emptied jerkily, a condition spoken of as "stammering" and apparently due to inco-ordination of the detrusor and sphincter musculature, or there may be some dribbling of urine at the end of micturition.

Paralytic incontinence may occur with cord lesions, more especially with those of the sacral segments, but this is comparatively unusual and is certainly not to be regarded as the inevitable outcome of bladder disorders.

It appears to be more likely to occur when, in nervous lesions involving the bladder, there is depression of the activity of the spinal cord, and of the bladder itself, from local infection and general illness.

(2) *Spinal cord injuries:* In severe injuries of the spinal cord, the bladder is at first paralysed and atonic and retention of urine results, with over-distension and overflow incontinence, unless catheterization is carried out.

After a period of weeks or months the bladder gradually recovers its tone and reacts to artificial distension by fluid run in through a catheter, by contraction of its detrusor musculature. At this stage, however, the internal sphincter still remains contracted and does not relax reflexly when the bladder fills with urine.

After a further variable period there is some reflex relaxation of the sphincter

and progressively increasing quantities of the urine are voided reflexly at intervals. The attainment of this condition is dependent on the absence of bladder infection and over-distension and on the presence of good general health in the patient [6].

Automaticity of the bladder is to be expected under these favourable conditions after complete transection and severe but incomplete injuries of the cord at any level compatible with life, even if the sacral part of the cord or the cauda equina is totally destroyed. In animals, indeed, it has been shown that automaticity may eventuate even after the removal of all nervous connections between the bladder and the central nervous system, though bladder evacuation is then relatively weak and the residual urine large.

Automatic activity implies, of course, an effective filling mechanism and is impossible when the sphincters are too relaxed to allow urine to collect in the bladder. The above facts imply therefore that a closed internal sphincter is possible in the absence of any nervous control from the spinal cord, and that an intrinsic mechanism exists which can relax the sphincter when the bladder is sufficiently distended. This inherent tonus of the internal sphincter is stated by Learmonth to depend upon a parasympathetic reflex. If this is so it must be a parasympathetic path lying wholly outside the central nervous system. In spinal transection which leaves a stump of spinal cord cut off from the higher centres, induced reflex activity of the mass reflex type results in emptying the automatic bladder, even though the contents are much below the volume usually required to effect a reflex evacuation, in other words reflex micturition is facilitated. Now this fact is an illustration of a general law which we owe to the acumen of Riddoch who states [7]:—

"All other portions of the nervous system with which a reflex arc is in communication influence its activity. Thus when spinal centres distal to the lesion were completely shut off from higher control the parts of the spinal cord with which a reflex arc was still in communication facilitated and augmented its activities; on the other hand when the distal portion of the cord was still connected with headward centres, so that postural reflex activities were exhibited, the influence exerted upon a reflex arc by the rest of the nervous system was one of inhibition and control."

We now see one reason why clinical records of disturbance of bladder function are apparently so contradictory. The same disease falling upon the same site in the cord will vary in its effects upon the bladder functions according to its severity and when sufficiently severe may actually give quite different bladder symptoms to those seen in the milder lesion.

It follows that while any connection exists between the reflex bladder centre, wherever that may be, and the higher parts of the nervous system, a connection sufficient to ensure the maintenance of postural reflex activities, then the micturition reflex will be held in "inhibition and control." It is the interference with the paths along which the inhibiting and controlling influences flow that causes the disorders of micturition seen in spinal disease, so different from those seen in lesions of the same structures that completely destroy them.

(3) *Disease and injury involving the sacral nerves.*

If the sensory or motor connections between the bladder and sacral cord are damaged but not destroyed, it would appear that the remaining nervous fibres prevent the establishment of automatic bladder function, and various types of bladder inco-ordination result: frequency of micturition, retention of urine, dribbling of urine from weakness of the sphincter, jerky or stammering micturition.

While the sympathetic vesical nerve supply remains intact some consciousness of bladder sensation may remain even when the sacral nerves or the parasympathetic connections in or outside the cord are destroyed, but there can be no doubt that bladder sensation, fullness, contraction, etc., are mainly conducted by the parasympathetic routes.

In tabes, neuralgic pains referred to the bladder region may be the first manifestation of bladder disorder. These may presumably arise at any of the posterior nerve roots conveying afferent fibres from the bladder, that is, from the ninth thoracic segment or higher, down to the fourth sacral. Other sensory disturbances of the bladder occur, irritability of the neck of the bladder leading to frequency, loss of knowledge of bladder fullness leading to retention with gross over-distention and overflow dribbling, and a marked atonicity of the bladder with trabeculation of the wall due to atrophy of the circular muscle fibres, perhaps partly trophic in origin. Section of the posterior sacral roots in animals results similarly in permanent abolition of micturition, permanent retention and frequent dribbling of urine.

In tumours of the cauda equina, if the conus is not involved, bladder disturbances are often absent, and when present are nearly always late in appearance. The first symptom usually is frequency of micturition, to be followed later by retention and then passive incontinence due to over-distension. After recoverable lesions persistent difficulty of micturition with much residual urine may remain.

If the conus *is* involved in tumours of the cauda equina, similar bladder symptoms appear early, or *suddenly* during the course of the disease [8].

Injury of the sacral nerves.—In cases of total destruction of the sacral nerves (parasympathetic path and pudic nerves) retention results, but after a variable period good and efficient reflex micturition is apparently established. Thus in a case of Riddoch's in which the tip of the conus and the whole of the cauda equina was believed to have been divided, automatic bladder action was established in four weeks: while in a case of Thomson Walker's in which complete destruction of the cauda was diagnosed retention persisted apparently indefinitely [9]. In 14 cases recorded by the latter in which partial injuries to the cauda were present, voluntary and normal micturition was retained in three, and in the remainder retention occurred followed in eight of them by the establishment of automatic reflex micturition. An appreciation that the bladder is distended may be retained in total injuries even when no knowledge of its emptying and no power to control its evacuation remain. This sensory stimulus must reach the cord through sympathetic channels.

The effects of injury to the sacral nerves illustrate well the difficulty which arises in co-ordinating experimental and clinical data. Barrington [10] has shown that if the pudic and pelvic (parasympathetic) nerves are sectioned in animals, urethral and sphincter resistance becomes minimal, so that urine constantly dribbles away when pressure is exerted on the bladder. These nerves include the whole of the vesical and urethral nerve supply from the sacral region of the spinal cord, and yet when all the sacral nerves are destroyed in man, or when the lower part of the spinal cord is completely excised in animals [11], retention results, followed ultimately by the establishment of "spontaneous" periodic micturition.

I have said sufficient to indicate the complexity of the problem and the fact that while we expect vesical disorder to follow severe lesions of the spinal cord and sacral nerves, our knowledge is insufficient to enable vesical symptomatology to be utilized for accurate localization of such lesions, or to permit us, as a rule, to associate specific lesions of the nervous system with unvarying and clear-cut vesical syndromes. An exception to this latter statement is necessary,—that of total transverse lesions of the cord.

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Dr. J. R. Learmonth (Section on Neurologic Surgery, the Mayo Clinic): I am happy to have the privilege of submitting for the consideration of the Section of Neurology, some recent work on the innervation of the urinary bladder in man. At the outset, it will be convenient to describe shortly the methods used in making the observations. All the observations on the bladder and on the urethra were made with the Braasch direct-vision cystoscope. During the experimental part of the work, the cystoscopist worked without foreknowledge of the procedures carried out on the nerves which were being investigated; and I am greatly indebted to Dr. Braasch and his colleagues of the Section of Urology in the Mayo Clinic for their willingness to carry out repeatedly what must have been a dreary mechanical task, as well as for other invaluable help. Occasionally it was desirable to make records of intravesical pressure for several hours; in such cases I used a kymograph. In many of the cases we made pre-operative and post-operative records of the physiological condition of the bladder by means of the Rose cystometer. All the intra-abdominal procedures were carried out under spinal anæsthesia, sometimes supplemented by a little nitrous oxide and oxygen. For stimulating the nerves I used a faradic current of sufficient intensity to cause a brisk twitch of the rectus muscle. Throughout the work I have had the constant advantage of the advice of my senior neuro-surgical colleague, Dr. Alfred W. Adson.

I propose to develop my subject in the following way: First, to give a brief description of the anatomical connections of the sympathetic nerve pathways concerned; second, to give the evidence at my disposal for each function that may be ascribed to the vesical sympathetic nerves, with, wherever possible, an account of clinical cases in which derangement of an individual function has been judged to be suitable for correction by the operation of sympathetic neurectomy; and third, to discuss briefly the functions of the parasympathetic and pudic nerves.

Sympathetic nerves to the bladder: Anatomical considerations.—By far the greatest number of the sympathetic fibres which reach the bladder traverse a stout nervous strand known alternatively as the presacral nerve (of Latarjet), or the superior hypogastric plexus (of Hovelacque). This structure is situated immediately under the parietal peritoneum, in front of the bifurcation of the aorta and the body of the fifth lumbar vertebra. It is described by Laux as having three roots, termed right and left lateral and middle, respectively. The lateral roots are made up of mesially directed branches from the first and second lumbar sympathetic ganglia, together with a smaller contribution of fibres derived from the semilunar ganglia and the renal plexuses, or the ganglia interpolated in the latter. After the juncture of its tributaries, each lateral root is continued downward and mesially towards the bifurcation of the aorta, where it approaches the opposite lateral root. The middle root is the downward continuation of the preaortic nervous network, which is derived from the upper abdominal sympathetic ganglia—the cœliac, semilunar, and aorticorenal. The presacral nerve varies widely in its architecture; it may assume any form, from a comparatively solid strand to a loose meshwork. After its formation the nerve receives, on each side, communicating branches from the third and fourth lumbar sympathetic ganglia. It continues its downward course into the pelvis, and about the level of the first piece of the sacrum it divides into the two hypogastric nerves. These join the postero-superior angles of the hypogastric ganglia; these ganglia are prominent, loosely constructed masses of nerve tissue situated on the lateral aspects of the rectum. In addition, they receive a few sympathetic fibres directly, from the third and fourth sacral sympathetic ganglia.

By patient dissection it is possible to isolate the various connections which have been described. The specimen illustrated is important from the standpoint of the central connections effected by the various strands. It is from a tabetic patient on whom I had performed rhizotomy of the right tenth, eleventh, and twelfth thoracic, and first lumbar, anterior and posterior roots. This patient died twenty-six days

after operation, as a result of the sudden occlusion of previously thrombosed pulmonary arteries. In conjunction with Dr. James W. Kernohan, neurological pathologist to the Mayo Clinic, I am studying the various filaments contributing to the presacral nerve, to determine the distribution of degenerated fibres. Although the presence of tabes introduces an element of uncertainty, we hope to obtain valuable information concerning the presence or absence of preganglionic and afferent fibres in the various strands.

Suitably stained sections of a presacral nerve at the level of the fifth lumbar vertebra show that roughly 60 per cent. of its fibres are medullated. Numerous ganglion cells are imbedded in its substance. Those medullated fibres which are efferent presumably have their synapses either in the hypogastric ganglia or in the intramural nervous apparatus of the bladder itself.

It is hardly necessary to remind you that not all the fibres in the presacral nerve are destined for the bladder; it is the pathway traversed by the sympathetic nerves for the contents of the pelvis.

To return to the hypogastric ganglia: in addition to sympathetic fibres in the hypogastric nerves, they receive also parasympathetic fibres, which are derived from the anterior primary divisions of the second and third sacral nerves. In and distal to the hypogastric ganglia, it is anatomically impossible to distinguish the sympathetic from the parasympathetic component of the nerve bundles.

On each side, the extrinsic nerves of the bladder leave the anterior borders of the hypogastric ganglia as five or six strands, which can be traced not only to the vesical walls, but also to the ureters, prostate gland, seminal vesicles and posterior urethra.

Since we are not immediately concerned with surgical problems, I shall not detain you by describing the operative exposure of the vesical nerves at different levels. I wish, however, to point out that although their connections are extremely intricate—so much so as to be a little bewildering—when they are viewed as a whole they have a physiological purposefulness in linking up every part of the urinary tract, so as to co-ordinate the formation and disposal of the urine. Clinically, certain "distant" symptoms of localized disease in the urinary tract may be a reflection of these widespread nervous connections.

Sympathetic nerves to the bladder: Functional considerations.—(1) The presence of inhibitory fibres.—I have not been able to demonstrate conclusively dilatation of the bladder on faradic stimulation of its sympathetic nerves. I have tried the experiment only on two occasions; the resulting variations in the capacity of the bladder did not seem to me of sufficient degree to justify any deductions. To be sure, in both cases the bladder was inflamed, and thus hardly suitable for the test; again, it may well be that by varying the intensity and the rate of the stimuli a combination would be found specific for inhibitory fibres. This is a matter for future trial. In the normally innervated healthy bladder, however, I have demonstrated active dilatation on pharmacological stimulation of its sympathetic nerves by the intravenous injection of adrenaline hydrochloride. I found that after the injection of 0·07 c.c. of a 1 : 1000 solution of adrenalin hydrochloride, there ensued an immediate active dilatation of the bladder, which retained its new increased capacity for about five minutes. Naturally the result of but one experiment cannot be more than suggestive.

The greatest and most convincing body of evidence regarding the presence of vesical inhibitory fibres has been accumulated clinically. My original presacral neurectomies were for paralysis of the bladder, due to a lesion somewhere in the parasympathetic (expulsive) system: and they were performed on the hypothesis that in such cases inhibitory sympathetic fibres, arising from more cranial intact segments of the spinal cord, might overbalance the reduced efficiency of parasympathetic fibres arising from damaged sacral segments of the cord. Let me illustrate this by the clinical features of two successful cases.

Case I.—A man, aged about 35, was affected with myelitis of the sacral segments of the cord, following an upper respiratory infection. He came to the Mayo Clinic a year later, on account of urinary trouble. He could micturate only with great difficulty and that in the sitting position alone. Residual urine was present to the amount of about 300 c.c. His convalescence following neurectomy of the presacral nerve was complicated by acute epididymitis; but on his recovery from this it was found that he could empty his bladder completely in any position. His cure has been maintained for nearly two years. A year after his operation we had an opportunity of examining him; his neurological signs remained unchanged; however, residual urine was absent, and intravenous urography disclosed a normal upper urinary tract.

Case II.—A boy, aged 8, had suffered, at the age of 3 years, from a form of paralysis which affected his lower extremities and his bladder. The highest affected segment of the spinal cord was therefore the second lumbar. Although the paralysis of the legs disappeared, that of the bladder persisted, and when I saw him he had been catheterized three times a day for five years; during this period the amount of residual urine had increased steadily. The result of presacral neurectomy was immediate, and has lasted for more than a year. The boy empties his bladder completely and is in excellent health.

I have operated in eight cases of this type. One patient failed to show any improvement and one cannot be traced. Of the remaining six, two are completely cured, three are much improved, the residual urine having been reduced from about 300 c.c. to about 20 c.c., and one is improved in so far as his expulsive mechanism is concerned, but has had recurrent attacks of seminal vesiculitis. The details of the case in which improvement did not follow the operation are instructive.

Case III.—A woman, aged about 58, suddenly became unable to pass urine. For three weeks before she came to the Mayo Clinic it had been drawn off at intervals. On examination she was found to have complete retention, and the cystoscope showed entire absence of expulsive force in the bladder. In order to verify this finding, on two occasions we tested the physiological condition of the bladder by connecting it to a kymograph. Even after the administration of large doses of acetylcholine the tracing did not register any contractions. In view of these findings she was kept for a period of two weeks on continuous drainage, and regular doses of acetylcholine were administered. At the end of that period a further test with the kymograph showed that some expulsive force was present. Accordingly, operation was advised and carried out. Much to my disappointment the condition failed to improve in the slightest degree. Her convalescence was complicated by recurring phlebitis in the left leg; when this local condition had subsided, a cystoscopic examination showed that although the expulsive force was considerably improved, the internal sphincter was still tightly contracted. In an effort to overcome this difficulty the sphincter was partially divided with a diathermy needle, and following this intervention the patient was able to pass urine voluntarily.

The lesson to be learned is, I think, that in certain cases the nervous lesion is intramural, and affects the terminal nervous apparatus, a possibility advanced many years ago by Sir John Thomson-Walker. In these circumstances, operations on the extrinsic nerves of the bladder are naturally of little benefit.

Although not one of these types of observation offers conclusive proof of the presence of inhibitory fibres in the sympathetic nerves, the combined evidence afforded by all appears to me to place their existence beyond any reasonable doubt.

(2) The presence of pain fibres.—At the beginning of one operation on the presacral nerve, I had occasion to grasp it with artery forceps. The patient at once complained of pain, which he described as "a crushing pain in the bladder." After section of the nerve, traction on its central end caused similar pain. In this case the effect of the spinal anæsthetic was passing off from above downward, and at the time of the observations the skin was analgesic only as high as the tenth thoracic segment. The impulses necessarily entered the spinal cord above this level, possibly along the branches of the splanchnic nerves. The closest questioning could not elicit that he felt any referred pain. There is thus fairly satisfactory evidence of the presence of pain fibres in this pathway. Clinical evidence in this regard has been available for a number of years, since for some time[1] surgeons have been

[1] The first presacral neurectomy for vesical pain was performed by Pieri in 1926.

dividing the presacral nerve for persistent pain in the bladder. Originally, a simple neurectomy was thought to be sufficient; Pieri has recently introduced a much more extensive operation, in which in addition to presacral neurectomy, the rami communicantes to the first three sacral nerves are divided on both sides. This is designed to interrupt all possible sympathetic pathways between the bladder and the central nervous system. I have operated eleven times for pain originating in the bladder; the results have been satisfactory in six of the eleven cases. The procedure seems to me to be a logical one, for two reasons: First, a certain amount of relief of pain should follow division of the afferent fibres in the sympathetic pathway; second, there should be an improvement in the local condition as a result of the vasodilatation which follows the operation. In this regard it may be noted that with the cystoscope it is possible to see vasoconstriction of the vessels of the bladder on faradic stimulation of the presacral nerve, and vasodilatation of these vessels after its division. The result of operation in these eleven cases was satisfactory in only six. There appears to me to be some ground for predicting that the operation is most likely to be successful when the lesions are confined to the trigone, since our more resistant cases have proved on analysis to have had some involvement of the dome. It is of interest to note that after this operation such ordinary sensibility as the bladder possesses is apparently unaltered; from the nature of the post-operative results it appears to me likely that the nerves which are divided are specially concerned with impulses set up by irregular and spasmodic contractions of the wall of the bladder. Continental observers report from this operation a much higher percentage of complete relief than I have found in my own practice, but I feel that even the more extensive operation leaves intact so many alternative paths for pain fibres that at best the results can be only incomplete. It is obvious that persistence of pain after these operations means that the parasympathetic pathway is richly supplied with pain fibres, as well as with afferent fibres conveying impulses of other types.

To sum up: There is evidence that a certain proportion of afferent pain fibres from the bladder traverse the sympathetic pathway. These are possibly concerned chiefly with the pain set up by irregular contractions of the bladder. The remainder of the pain fibres, and other afferent fibres, reach the central nervous system along the parasympathetic pathway.

(3) Presence of motor fibres to the internal sphincter.—There is, of course, nothing new in the idea that the motor nerves of the internal sphincter are sympathetic in origin; Gaskell held that this arrangement was typical for all vertebrates. I have been able to show that in man faradic stimulation of the presacral nerve results in a strong contraction of the sphincter, which may be observed from the posterior urethra, or deduced from the tightness with which an instrument introduced into the bladder is grasped by the contracted muscle. The same result is obtained on stimulation of either hypogastric nerve, or of a lateral root of the presacral nerve. After division of the presacral nerve the sphincter relaxes, but after some days it recovers considerable tone; later in this paper I shall return to this point.

In two cases I have availed myself of this finding, in the treatment of spasm of the sphincter. The details of one of these will be sufficient.

Case IV.—A man, aged 58 years, for ten years had had increasing difficulty in starting the flow of urine. Finally he was able to urinate only after introducing a small quantity of hot water into the rectum. He himself was convinced that difficulty in relaxing the sphincter was the cause of his condition, and cystoscopic examination failed to disclose any organic obstruction at the neck of the bladder. Several local operations had been performed elsewhere, without affording him any relief. The effect of division of the presacral nerve was immediate; even in bed he did not have any difficulty in urinating, and he felt that the "spasm" of which he complained had been relieved. This relief has been maintained for several months.

In both cases I felt that the vesical difficulty was due either to hypertonus of the internal sphincter, or to inco-ordination of the nervous mechanism which secures relaxation of this structure at the beginning of micturition.

(4) Motor fibres to the muscle at the uretero-vesical orifice.—Following stimulation of the presacral nerve both uretero-vesical orifices contract until the openings have a pin-point appearance. Stimulation of the distal end of a cut hypogastric nerve produces the same effect on the ipsolateral orifice. To the best of my knowledge the peri-ureteral muscle at this point is not thickened to form a special sphincter ; possibly the effects described are to be attributed to the response of the trigone to stimulation of its sympathetic nerves, which will now be considered.

(5) Motor fibres to the trigonal muscle.—Stimulation of the presacral nerve, or of either hypogastric nerve, results in a contraction of the trigonal area of the bladder. To the eye of an observer, this contraction is easily distinguishable from, for example, the rapid, firm contraction of the internal sphincter, which also follows the stimuli. The trigonal contraction is a much slower affair, and seems to be a gradual taking-up-slack in the area concerned. We were much interested in this simultaneous contraction of the trigone and the internal sphincter. It had been suggested by Young and Davis that at the beginning of micturition the internal sphincter is opened mechanically by the pull of extensions of the trigonal musculature, which pass within the grasp of the sphincter to insertions in the posterior urethra. In this regard, there is a possibility that at the beginning of the act fibres for the trigone alone are in action, but from other evidence it seems more likely that the opening of the internal sphincter is due to inhibition of its natural tonus. To this point I shall return.

After sympathetic neurectomy the trigone, at least in the male, becomes flaccid and atonic. This relaxation may be so pronounced that an ounce or so of residual urine may collect in this trigonal sac, but we have been able to permit the bladder to get rid of this residue by dividing the posterior margin of the internal sphincter, a small operation which provides a continuous channel from the trigonal pool.

We are accumulating a certain amount of evidence which suggests that the innervation of the trigone is different in the two sexes. My urological colleagues report thst after sympathetic neurectomy the relaxation of the trigone is never so marked in female patients as in male patients ; indeed, it may be absent.

(6) The behaviour of the internal sphincter after sympathetic neurectomy.—In those cases in which sympathetic neurectomy is performed on patients with normally innervated bladders, the internal sphincter is at first dilated ; but in the course of two or three weeks it recovers sufficient tone to close more or less completely, although its resistance is readily overcome by the point of an instrument. This recovery of tone on the part of the sphincter has interested me more than any other problem which has arisen in the course of the investigation. Obviously, there must be a local intrasphincteric neuromuscular apparatus which is adequate to maintain at least a proportion of tonus. You remember that Gaskell held the view that preganglionic sympathetic fibres destined for the plain sphincters of the alimentary and urinary tracts, had their synapses in the sphincter itself. If this is the anatomical arrangement, after division of the presacral nerve, the postganglionic neurone of the sphincteric nerve supply is intact, and is sufficient to produce some tonic effect. By a process of exclusion, the afferent limb of the reflex arc concerned must traverse the parasympathetic pathway.

(7) Effect on micturition of division of the sympathetic nerves to the bladder. —For a few days following sympathetic neurectomy it is not uncommon for some frequency to be present ; this has been attributed to division of inhibitory fibres. Thereafter the act is in every way normal, and the operation may be undertaken without fear of disturbing vesical function.

(8) Effect on micturition, in the female, of dividing the pudic nerves.—Some four years ago Wertheimer and Michon advocated division of the pudic nerves in cases of kraurosis vulvæ or of pruritus vulvæ; they reported that this operation was without effect on vesical function. I have performed this operation several times, and can confirm the postoperative absence of any interference with micturition. It is probable, therefore, that in the female both the storage and the discharge of urine can be exercised by autonomic nerves alone. After operation, these patients can start and stop the flow of urine at will, so that it is possible for the will to be exercised along autonomic paths. Moreover, the response of the bladder to the introduction of fluid, as tested by the Rose cystometer, is indistinguishable from the normal response.

It follows, that in women only the parasympathetic pathway is indispensable for the act of micturition.

Collateral effects of sympathetic neurectomy.—(*a*) In the female.—It is of interest that conception, normal pregnancy, and normal delivery have followed division of the presacral nerve in women. Occasionally the operation is followed immediately by menstruation; doubtless this is the result of the general pelvic vasodilatation which follows interruption of the constrictor fibres in the nerve.

(*b*) In the male.—Early in my investigations it was noted that when the presacral nerve was stimulated, a cloud of seminal fluid and prostatic secretion was poured into the prostatic urethra; therefore the nerve must supply motor fibres to the musculature of the seminal vesicles, the ejaculatory ducts, and the septa of the prostate gland. It is of great physiological interest that, following sympathetic neurectomy, male patients have found that although they could perform the sexual act, and although they experienced a psychical orgasm indistinguishable from the normal, ejaculation did not occur. Now it is known that after the operation of lumbar sympathectomy, in which the second, third and fourth lumbar ganglia, together with the intervening trunks, are removed, such an alteration of sexual function is absent. It would appear, from a process of exclusion, that the motor fibres for the genital structures in question are derived from the first lumbar ganglia. It may also be concluded that the sensations constituting the orgasm are not directly associated with contractions of the seminal vesicles and ejaculatory ducts. Obviously also, male patients must be warned before operation that following it they will be sterile, although not impotent; this fact must influence the choice of operation, when it is important to secure a succession.

To conclude: there are still many unknown and many debatable features of vesical innervation in man. However, as a result of this work, I feel that several points have been clarified and established. Finally, I wish to insist most emphatically that the development of operations on the nerves of the bladder does not enable the surgeon to play the part of a therapeutic god-from-the-machine in obscure conditions of vesical dysfunction. In selected cases they offer a useful addition to recognized urological procedures; but I would be sorry to see them undiscriminatingly employed without the close co-operation of a critical urologist, or without adequate neurological investigation. Only because I have had such invaluable co-operation have I ventured to present to you the details of my clinical cases.

Mr. F. J. F. Barrington: I propose giving a summary of the conclusions from experiments on the nervous mechanism of micturition in the cat, the animal on which most observations have been made.

The efferent nerves arise from part of the lumbar and part of the sacral regions of the cord. Spinal roots sending no fibres to the bladder intervene between these two groups of spinal roots which supply such fibres. This arrangement exists in all mammals which have been examined and also in the frog and the toad. The lumbar efferent nerves are part of the sympathetic. From the white ramus of each lumbar nerve concerned, a branch, the lumbar splanchnic nerve, passes through the

sympathetic to the inferior mesenteric ganglia; from these ganglia two nerves, the right and the left hypogastrics, pass backwards into the pelvis where each divides and anastomoses with branches of the sacral nerves, forming the pelvic plexus from which branches are distributed, among other organs, to the bladder and the urethra. Sacral efferent nerves arise by branches from the ventral surface of two or three sacral nerves which unite into a trunk—the pelvic nerve, or erigens, which passes ventrally, splits up, and anastomoses with branches of the hypogastric nerve to form the pelvic plexus. The pudic nerve is an efferent nerve concerned with micturition in that the compressor urethræ is supplied by a branch of the dorsal nerve. The compressor urethræ being a striped muscle, the fibres of the pudic nerve are not interrupted by ganglion cells between its origin and its end. Each efferent fibre of the pelvic and of the sympathetic nerves is at one point interrupted by a ganglion cell. In the sympathetic nerve most of the bladder fibres have their ganglion cells in the inferior mesenteric ganglia, but this is not the case with fibres distributed to all of the other organs which it supplies. The ganglia of the pelvic nerve fibres are situated distally, on or near the organs supplied. The fibres of the pelvic nerve are therefore pre-ganglionic, while the bladder fibres of the hypogastric nerve are chiefly post-ganglionic; this is also true of the dog. The hypogastric, the pelvic and the pudic nerve all contain afferent as well as efferent fibres.

Stimulation of the peripheral cut end of one pelvic nerve produces a powerful contraction of the bladder. This experiment has been made on several other mammals, with the same result. Stimulation of the peripheral cut ends of both hypogastric nerves produces a small transient diminution in the bladder volume, followed by a slow and considerable increase: the initial diminution is due to contraction of the muscle at the base of the bladder. Stimulation of the hypogastric nerves has been carried out on several mammals and found to give rise to effects on the bladder volume which vary greatly in different species. The smooth muscle of the urethra contracts as the result of the stimulation of the hypogastric nerves and relaxes as the result of stimulation of the pelvic nerves.

Division of both pelvic nerves is followed by retention of urine with unconscious overflow. The animal does not behave as if it were in pain and the bladder is not tender on pressure, although its own internal pressure may have injured it so severely as to have produced extravasation of blood into its walls. The same condition arises in the dog. After some days a cat with both pelvic nerves divided becomes conscious of wanting to pass urine and passes small amounts at short intervals for certain periods, holding its urine for long intervening periods, but it always has a considerable volume of residual urine; this condition is permanent. If the pudic nerves of such a cat are divided, the urethral resistance and the volume of residual urine diminish, retention with overflow appears again and the cat is no longer conscious of a desire to micturate. A permanent condition exactly resembling that following the division of both pelvic nerves in the cat, is seen at times after excision of the rectum in man. The chief afferent nerves concerned in micturition, including those which give rise to the pain of retention of urine, must therefore pass to the cord in the pelvic nerve, while the remainder pass in the pudics. It cannot, however, be inferred from this that the pain due to certain pathological processes in the bladder does not travel in the afferent fibres in the hypogastric nerve.

Division of both hypogastric nerves in no way interferes with the normal performance of micturition: this is also true for the dog. A slight degree of frequency of micturition arises which continues to increase at least for some weeks. It appears, therefore, that some progressive condition, such as might he brought about by a vascular alteration, must be produced by division of the nerves as well as the simple removal of an inhibitory tone. Division of the hypogastric nerve does not lead to a permanent weakening of the smooth muscle of the urethra, at any rate of such a

degree as to allow the bladder to force urine through the internal urinary meatus at other times than during micturition.

Division of both pudic nerves produces a slight degree of incontinence which usually is only evident by the escape of urine if the bladder is gently squeezed, but occasionally may be severe enough to lead to the escape of a few drops of urine whenever a straining movement, such as jumping, is made.

Division of the dorsal spinal roots in the sacral region is followed by retention of urine, with unconscious overflow incontinence. This also occurs in the dog. The compressor urethræ remains firmly contracted. The condition is permanent.

Lesions of the peripheral nerves, therefore, show that a complete disorganization of micturition results from the destruction of the sacral nerves, or even of their afferent fibres, whereas micturition remains unimpaired after the destruction of the sympathetic nerves, although these have an effect on the bladder and urethra. It seems not improbable that this arises from the fact that the urethra of a male mammal is used for ejaculation as well as for micturition and that the effects of the sympathetic on the bladder and urethra are for use in ejaculation and inherited in both sexes. This seems more probable in that the effect of the sympathetic nerves on the bladder in various species of mammals is very variable, whereas that of the sacral nerves is very constant. The sympathetic is the efferent nerve for most of the obvious factors in ejaculation in all such mammals have been examined, the hypogastric being the motor nerve to the vas and to the vesicula seminalis and the secretory nerve to the prostate and to Cowper's gland. The fact that the arrangement of the bladder nerves is apparently the same in the frog as in the mammal appears to be against this supposition, but very little experimental evidence exists as to how a frog's bladder is emptied and none at all as to how it is filled.

When decerebration is performed in the usual way, the plane dividing the brain commonly goes through the superior colliculus above, and the crus, at about the emergence of the third nerve, below. Most of such cats pass urine in considerable quantities at long intervals, without any residual urine. When this is not the case there are generally other well-marked signs of failure of function of the brain behind the section, such as disappearance of rigidity or gross changes in the respiration. In the cat, therefore, all parts of the central nervous system necessary for the performance of micturition must be behind the level of a plane through the middle of the superior colliculus above and of the middle of crus below. Since micturition is a function which can be largely affected by volition, it would not be safe to infer that the same is true in man.

When a decerebrate cat's bladder is filled with water at a pressure of 10 cm. it shows rhythmic contractions : a transection across the medulla abolishes the contractions and leads to a great and lasting dilatation. The transection is therefore at or behind a part of the brain from which the reflexes of contractions are taking place. If a number of cats are treated in this way, making the transections at different levels, it is found that transections behind a plane going through the posterior part of the inferior colliculus dorsally and the middle of the pons ventrally always lead to the abolition of the reflex contractions, while those in front of this plane commonly do not. The part of the brain concerned with the contractions is therefore in this plane.

A series of cats with bilateral lesions in this part of the brain, made by electrolysis with a Clarke's stereotaxic instrument, showed that permanent residual urine followed bilateral lesions situated just ventral to the internal edge of the superior cerebellar peduncles from the level of the anterior end of the motor nucleus of the fifth nerve forwards to the level of the posterior end of the aqueduct, but did not follow bilateral lesions close to this position but not actually involving it. These cats all retained a consciousness of wanting to micturate. Bilateral lesions of the

ventral half of the sides and of the floor of the posterior end of the aqueduct lead to loss of consciousness of a desire to micturate without residual urine. The lesion producing this condition overlaps in level that producing residual urine posteriorly, but it is nowhere continuous with it, being more dorsal in position. For this reason it seems probable that the cats with residual urine retained their consciousness of a desire to micturate because the essential part of the brain in their case was incompletely destroyed.

By dividing the bladder neck in a decerebrate cat, tying a cannula into each cut end and connecting the cannulæ with the appropriate instruments for measuring volume and pressures, two hind-brain and three spinal reflexes can be found. Both the hind-brain reflexes result in a strong contraction of the bladder; the first is evoked by distending the bladder and has both its paths in the pelvic nerve. The second is evoked by running water through the urethra and has its afferent path in the pudic and its efferent in the pelvic nerve. The third reflex, which is spinal, results in a feeble, transitory contraction of the bladder; it has both its paths in the hypogastric nerve and is evoked by distending the urethra proximal to the compressor urethræ. Both the fourth and fifth reflexes are spinal, effect a relaxation of the compressor urethræ, and have their efferent paths in the pudic nerve; the fourth is evoked by running water through the urethra and has its afferent path in the pudic nerve, while the fifth is evoked by distending the bladder and has its afferent path in the pelvic nerve. By a rather different method it can be shown that there is a sixth reflex which is spinal, has both its paths in the pelvic nerve, is evoked by distending the bladder and effects a relaxation of the urethra proximal to the compressor urethræ. It will be seen that in most cases the effect of one reflex will elicit the others and that, as far as is known, the only reflexes giving rise to a strong contraction of the bladder are abolished by a spinal transection.

Micturition is affected in the same way, by spinal transection, whatever its level, provided it is not so far forward as to be incompatible with prolonged life or so far backward as to involve the nucleus of the pudic nerve. The bladder gradually fills and becomes over-distended and urine drips away in small quantities nearly continuously. The urethral resistance at this time is very great. Perineal contractions can be evoked by pressing on the bladder before—and occur spontaneously after—it has become over-distended. At the end of a week there is a marked diminution in the urethral resistance and in the volume of residual urine; both these are further diminished by the end of the second week. From this time onwards the condition does not alter. The cat holds urine for considerable periods, passes it in a series of rhythmic jets which are associated with, and have the same periodicity as, a series of rhythmic perineal contractions; residual urine is always present. The passage of urine in this way, and the perineal contractions, are readily evoked by almost any cutaneous stimulus near the perineum, and by anything calculated to increase the pressure in the bladder or proximal part of the urethra, such as holding the cat vertically. If the bladder is gently squeezed, urine escapes in jets and the urethral resistance can be felt to alter rhythmically.

The most striking alteration which occurs in the transition from retention with overflow to the final stage, or so-called automatic micturition, is the diminution of the urethral resistance: it appears probable that all the other alterations are secondary to this. In an intact cat, although the compressor urethræ is the part of the urethra most firmly closed, urine is held at the internal meatus; this is also true for the dog and for man. After a spinal transection and also after division of both pelvic nerves, or of the dorsal spinal roots in the sacral region, urine is held at the compressor urethræ and the proximal part of the urethra is full of urine. Urethral resistance after a spinal transection, whether recent or remote, nearly vanishes after division of the pudic nerves. The diminution in the urethral resistance which occurs in the first two weeks after a spinal transection is therefore due to a diminution in

the contraction of the compressor urethræ. If both pelvic nerves are divided at the time of the transection, the diminution in the urethral resistance is prevented, and if after a transection it has occurred, division of the pelvic nerves restores the urethral resistance to its original strength. The diminution in the urethral resistance which follows a spinal transection is therefore due to an increased activity of the fifth reflex, and not to weakening of the compressor urethræ.

Mr. A. Ralph Thompson drew attention to three points that had not been noticed in the previous communication.

First, a sense of irritation was present at the end of the penis when there was a desire to micturate, and this was exaggerated in cases of bladder frequency which might be due to stone and cystitis. He thought that a stimulus producing the act of micturition came from the end of the penis.

Secondly, though there might be an internal sphincter, he was not prepared to believe that it was a localized sphincter, but he believed that any part of the bladder might act as an internal sphincter. He had drawn attention already to one case in which this supposition was practically proved.[1]

Thirdly he thought that the fact that semen could be discharged when the bladder was full of urine was against any very great influence of the "compressor urethræ" muscle in connection with the control of micturition.

Mr. John Everidge: With regard to Mr. Ralph Thompson's remarks as to the inability of the external sphincter (the compressor urethræ) to retain urine within the bladder, Sir John Thomson-Walker has definitely proved the contrary to be the case, as illustrated in the surgery of the enlarged prostate. In such ne has shown that the internal sphincter, deranged in function either by the previously enlarged prostate or by the operation of suprapubic prostatectomy, ceases in many cases to function, and that it is upon the compressor urethræ alone that the patient depends for continence.

Dr. George Riddoch pointed out that automatic micturition might occur after a lesion of the cauda equina, and in such cases also all vesical sensibility was not lost, as the patient might be aware when his bladder was full. Some sensory afferents evidently entered the cord by the hypogastric nerves. Vesical sensibility was abolished by a lesion of the spinal cord at the eleventh thoracic segment.

[1] *Proceedings*, 1931, xxiv (Sect. Urol., 47-53).

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The Bearing of Recent Research on the Sex Hormones on Clinical Obstetrics and Gynæcology.

By Professor E. C. Dodds, M.V.O., M.D.

There has been more rapid development in the field of sex hormone research during the last few years than in almost any other branch of medicine. In fact, the publications have multiplied so rapidly that it is almost impossible for any person to be up to date, or at any rate to be so for any length of time. Fortunately there is a series of full reviews on this subject, and consequently I do not intend to take up valuable time by going over in any detail the historical aspects. One might perhaps point out that the classical researches of Marshall and his school succeeded in clearing up a great deal of the chaos associated with the question of the reproductive cycle of animals, but that following his pioneer work no advance of any note was made until the American workers, Allen and Doisy, combined some of the older chemical work on extracts of the ovary with the more modern biological work done in Professor Stockard's laboratory in New York. It will be remembered that the latter observer and his co-workers demonstrated that the alternating periods of sexual activity were accompanied by definite changes in the microscopical character of the vaginal smear, so that with experience it would be possible for any observer to state at exactly what period of the œstrous cycle the animal happened to be. Removal of the ovaries causes an absence of the cyclical changes, so that the animal remains in a permanent state of di-œstrus. Allen and Doisy applied this principle to the standardization of crude extracts of the ovary. They showed, for instance, that an alcoholic extract made from the ovary was capable of restoring the cyclical changes in a castrated rat or mouse when injected subcutaneously. Here, then, was a method whereby the potency of the experimental ovarian preparations could be investigated, and, as was to be expected, an entirely new series of experiments arose from these observations. Through this work it was possible to prepare highly potent extracts and to gain considerable insight into the biochemical characteristics of the œstrus-producing hormone.

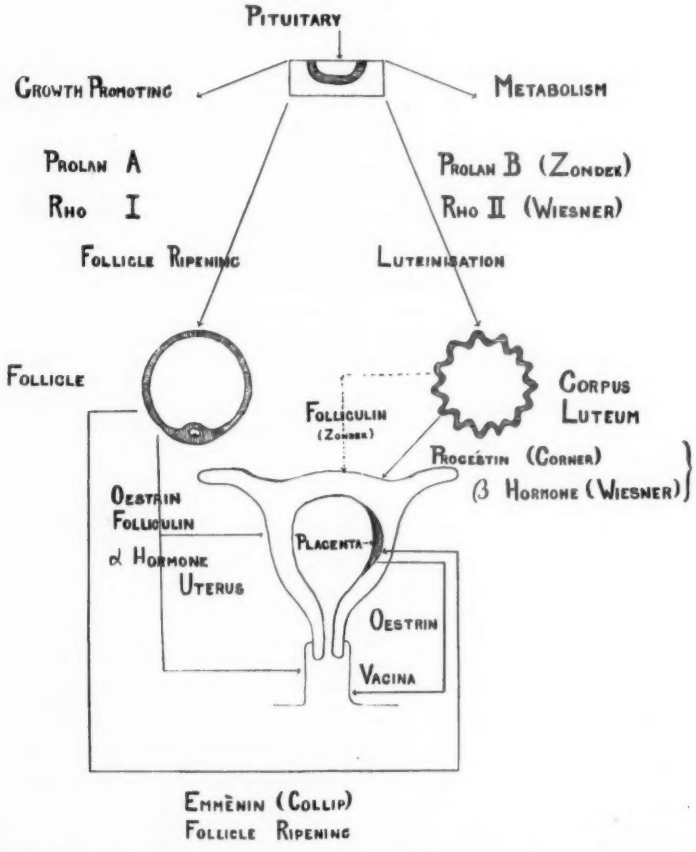
The next great stimulus to research in this field was provided by the discovery of the German workers, Aschheim and Zondek, that œstrin, to give it its most generally accepted name (though Wiesner calls it the Alpha hormone) is excreted in the urine during pregnancy. This gave the biochemists a source for the material, and by a relatively simple application of chemical technique it was possible to obtain very large quantities of the active principle without its being contaminated with unpleasant impurities such as are encountered in extracts of the ovary or placenta.

Yet another stimulus was added by the researches of the American workers who demonstrated the effect of transplants and extracts of the anterior lobe of the pituitary upon the sex cycle. These experiments were performed by Aschheim and Zondek, and by Smith and Engle, almost simultaneously. They showed that these pituitary transplants were capable of causing premature puberty with the development of œstrus and luteinization of the ovaries in immature animals. Again, the demonstration by Aschheim and Zondek of the presence of this luteinizing substance in the urine of pregnant women laid the foundation for a long series of observations stretching from purely chemical considerations of the hormone, on the one hand, to the establishment of an accurate test for the diagnosis of pregnancy, on the other.

Finally, the careful morphological and histological observations of Corner led him to prophesy with great accuracy the possible action of the corpus luteum hormone. Some few years ago he announced the method for the extraction of this internal secretion from corpora lutea and he demonstrated its action upon the uterine mucosa of animals such as the rabbit.

Before proceeding further it will perhaps be advisable for me to give a rapid diagrammatic sketch of the present-day views with regard to the interaction, etc., of this hormone. Great care will be taken only to include details which are based upon actual experiments, and not, at this stage, to indulge in the purely speculative side of the subject.

The following diagram, modified from the publications of Zondek, will serve to give a rough idea of the present-day views.



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The ovarian periodicity we believe to-day to be due entirely to the action of the anterior lobe of the pituitary, which may be regarded as the stimulus or starting mechanism. It is believed that the anterior lobe of the pituitary secretes hormones which affect firstly growth, secondly metabolism, and thirdly sexual functions. With the two former we will not concern ourselves here. The function of the sex-fraction is to stimulate the ovary, thus causing ripening of the follicles, followed by rupture and hæmorrhage—in other words, the formation of a corpus hæmorrhagicum and the ultimate conversion of this into a corpus luteum. This hormone is referred

to as "Prolan" by the German workers, and as the "Rho" factor by Wiesner. Originally it was said to consist of two factors, one responsible for the follicle ripening (called by the Germans Prolan A, and by Wiesner Rho 1) and the other responsible for luteinization (known as Prolan B or Rho 2). It would appear, however, that the separation of the two was more theoretical than practical, although I must point out that there are many authorities who still believe in the separate identity of these two fractions. It is only fair to add, however, that all the methods of separation which have been published have failed to work in the hands of impartial observers. The stimulated ovary, with ripening follicles, secretes œstrin, which causes enlargement of the uterus and puberty, together with the opening of the vagina and cornification of the vaginal epithelium—which are characteristic of œstrus. The corpus luteum, on the other hand, secretes another hormone which is called by Corner "Progestin" and by Wiesner the "Beta" hormone. This hormone produces pregestational changes in the uterine mucosa, and together with œstrin, is capable of causing great enlargement of both the musculature and the mucosa of the uterus. Expressed very briefly, it would appear that Progestin is responsible for the development of the decidual changes, and is probably the hormone responsible for the phenomenon of pseudo-pregnancy.

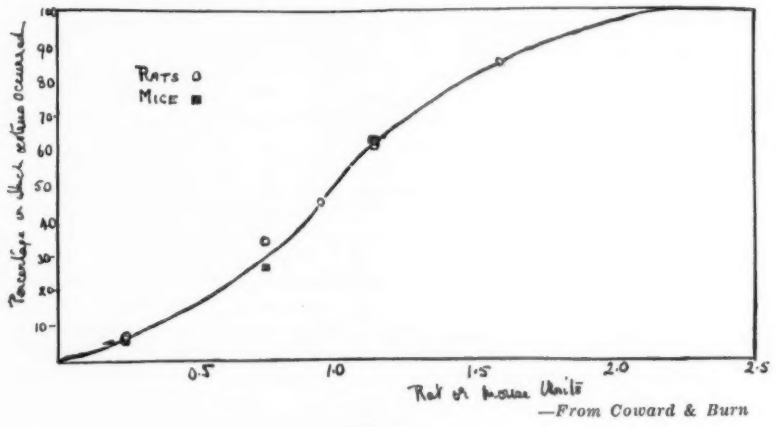
Up to the present, we have not dealt with any controversial matter and I feel fairly certain in saying that there is no one in my audience who will get up and contradict anything which I have so far said, with the possible exception of the remarks about the separation of Prolan A and B. We now have to turn to a series of hormones whose position is not as clear as that of the three already mentioned, namely, œstrin, Prolan, and Progestin.

Collip in Canada has succeeded in preparing an extract from the placenta which stimulates the ovary in a manner very similar to that of Prolan. This substance, which he calls Emménin, he believes to be an entirely new principle, free from œstrin, and quite distinct from Prolan. Other workers, however, tend to regard it as being identical with Prolan.

A further demonstration of the interaction between the various glands mentioned can be found in castration experiments. For example, if both ovaries are removed very definite changes appear in the anterior lobe of the pituitary, with the development of a certain type of cell known as a castration cell. The appearance of these cells can be prevented by the injection of œstrin subcutaneously into the animal, so it would seem that whilst the anterior lobe of the pituitary has a profound action upon the ovary, the products of the reaction of this substance also affect the pituitary, e.g., œstrin in turn affects the anterior lobe of the pituitary. That the position is extremely complicated there can be no doubt at all, and one of the most important problems upon which to speculate is the cause of the cyclical changes. In other words, why should the pituitary produce this follicle-ripening material at a fluctuating rate? The modern German writers have developed an interesting theory—but here a word of warning must be given that it is purely speculative. One can say, however, that like other stories it is "founded on fact." It is assumed that the anterior lobe of the pituitary begins to secrete Prolan, which in turn stimulates the ovary to secrete œstrin. Through the prolonged action of the Prolan a corpus luteum is formed and in time this corpus luteum begins to secrete Progestin. The Progestin then re-acts on the anterior lobe of the pituitary and reduces the secretion of Prolan so that the corpus luteum retrogresses. When the corpus luteum has retrogressed we get an immediate re-establishment of the secretion of Prolan, and so the process goes on. It is not very difficult to think out some very serious arguments against this otherwise highly attractive theory. For example, it will not explain the enormous production of œstrin and Prolan during pregnancy, when presumably the corpus luteum is also continuing to secrete Progestin. Again, the state of affairs in pregnancy appears to be almost inexplicable. Thus, many cases have been recorded

in the literature in which the removal of both ovaries has not been accompanied by termination of the pregnancy. I have been informed by gynæcologists that neither destruction nor complete excision of the corpus luteum during pregnancy terminates the condition, and lactation, etc., has occurred quite profusely after a normal delivery. In my own laboratory, Allan and Wiles have succeeded in removing the anterior lobe of the pituitary in pregnant animals without the development of any dramatic symptoms. It is a great pity that there is no record of a study of the excretion of the hormones in the urine in women from whom both ovaries have been removed during pregnancy. It is hoped that should any member of the audience have such a case he will see that the urine is carefully examined.

The difficulties, however, are not at an end at this stage. There are many other factors controlling the action of a hormone such as œstrin. For example, workers in this field have been hampered for many years by the difficulty of finding an accurate quantitative method of estimation. It has been demonstrated that the substance cannot be standardized by injecting it from the point of view of determining the minimum quantity necessary for the production of œstrus in a single castrated animal. The following curve



—*From Coward & Burn*

FIG. 1.

shows the experiments of Coward and Burn. Along the base line is plotted the percentage of each of the groups showing œstrus, and it can be seen that as the amount injected is increased, so an increasing percentage of rats or mice shows œstrus. The curve, however, flattens out very considerably before the 100% is reached. That is to say, a point can be taken on the curve at which it is possible to give, let us say, 100 rats equal doses and 50% of them will show a complete œstrus, whereas 50% of them will not. By common consent, therefore, this has been taken as the standard unit in this country.

Other points to be dealt with are the purity of the material and the mode of administration. If the material is very active, then it must be given in a series of divided doses. This can be explained by the fact that the highly potent substance is rapidly excreted from the animal. In proof of this statement may be seen the effect of emulsifying the material with oil. Fig. 2 illustrates this point.

Up to the present, I have referred entirely to subcutaneous injection. Turning to the very difficult problem of oral administration, it was agreed at one time by most workers that the œstrus-producing hormone was inactive when given by mouth,

but further researches have shown that the efficacy of the preparation depends again upon the purity and the mode of administration. Fig. 3 illustrates the effect of increasing dosage in a series of groups of rats when given by the oral method.

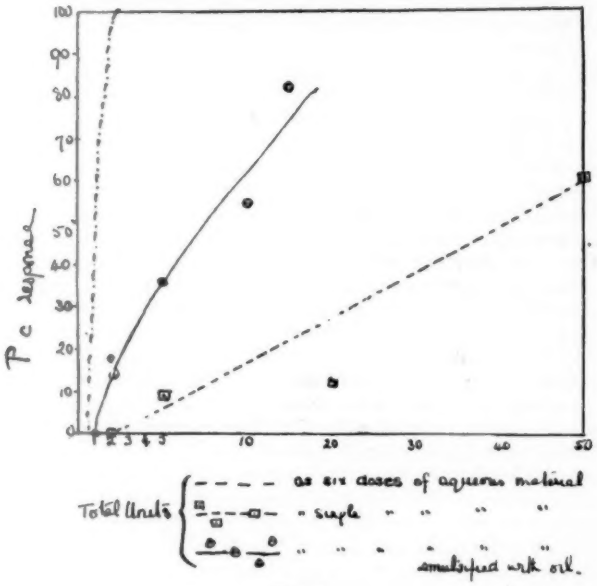


FIG. 2.

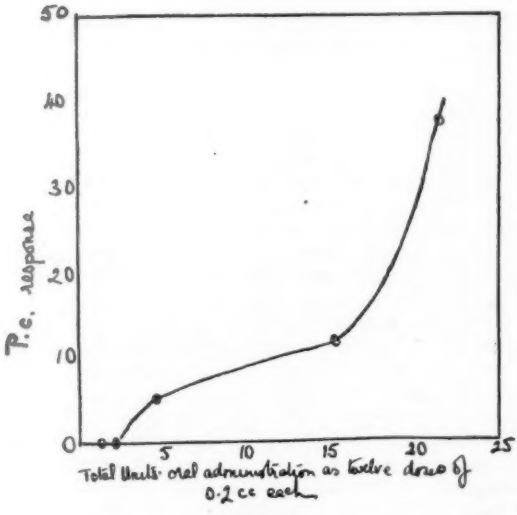


FIG. 3.

As can be seen, to produce 50% response it is necessary to give over 25 times the quantity required to produce œstrin by subcutaneous injection. Another interesting fact is that the cruder the material, the more active it appears to be by mouth. The following table shows that the crystalline material requires 58 units to produce œstrus in 50% when administered orally, whilst the crude material at 200,000 units per gramme, only requires six.

Mouse units per G.	Number of units required to produce œstrus in 50% of animals when administered orally.
8,000,000 (crystalline)	58
1,000,000	30
200,000	6

This very brief summary of the present position with regard to the œstrus-producing hormone does not attempt to embrace the wonderful advances which have been made in the study of the chemical constitution. Turning to the other hormones, we can see that the chemical researches on the constituition of Prolan have not advanced to anything like the same degree as those with œstrin, since this hormone is a nitrogen-containing substance of an extremely complicated type. The hormone of the corpus luteum has been, relatively speaking, little studied, owing to the great difficulty of obtaining sufficient quantities of the material. The yield is very poor from the admittedly difficult starting material, and it appears unlikely that any marked developments will occur in the chemistry of this substance in the near future.

I have not lost sight of the subject for discussion this evening, namely, the bearing of research on the sex hormones upon clinical work. We can state definitely that out of these researches has been evolved an accurate, rapid test for the diagnosis of pregnancy. As, however, this has been discussed so many times before, I do not propose to discuss it here. In view of what we have said with regard to the difficulties of standardization, etc., I cannot help feeling that all the clinical work which has been done in the past with the sex hormones may be disregarded. In the first place, there can be no doubt that the amounts of material used have been grossly inadequate. Most observers would agree that the amount necessary to produce œstrus varies, roughly, in proportion to the body weight of the animals. Thus, in a series of experiments done on the relationship of the rat and mouse units in two different laboratories, it was found that the rat unit was 10 times the mouse unit, and that the ratio of the weights was exactly 10 : 1. It follows that on this basis a very great deal of material will be required to produce any changes in the human subject. Dr. Parkes will tell you later of his important observation that some 300 units are required to produce the uterine changes in the rat which are characteristic of true natural œstrus, the criterion taken of perfect œstrus being that copulation and the formation of vaginal plugs will take place. This, as I stated, requires some 300 units. He will also tell you of his experiments with baboons and the very great amount of material required to produce the external signs of œstrus. If one looks through the literature one will find that those observers who have employed carefully standardized material have only used some 10 units per day. The definite opinion of all reliable workers is that the results with such dosage are inconclusive. Assuming that sufficiently large doses can be given, one again comes to the question of dealing with the absorption. I am at present experimenting with esters of œstrin and am attempting to give 20,000 units to patients. Unfortunately, it is too early as yet to assess the value of this treatment. The question arises as to what are the indications for the administration of these three hormones? Œstrin has been seriously recommended in all types of menstrual disorder, in every type of insanity, in endarteritis obliterans in men, in Berger's disease in men, in hæmophilia, in retinitis pigmentosa and in many other conditions. Prolan has also been recommended in every type of menstrual and gynæcological disorder, and in addition, in baldness in men. The corpus luteum hormone, Progestin,

has also been recommended for every gynæcological complaint, but owing to the difficulty of obtaining it, it has not yet been tried in conditions such as urticaria, megalomania, etc. I would suggest that in the early stages, at least, of this new experimentation, one should deal solely with clear-cut cases, the most important, to my mind, being those of young women in whom both ovaries have been removed and the uterus left. If a collection of such cases could be obtained, then it would be possible to conduct carefully controlled experiments with the various hormones. I cannot help feeling that the majority of the papers published up to the present, and particularly those which claim that by the use of these hormones, and more especially œstrin and Prolan, every form of amenorrhœa and menorrhagia can be controlled, are definitely untrue. There are many papers, however, from reliable sources in America and Germany on the use of the corpus luteum hormone in cases of habitual abortion. It is claimed that when doses as small as 70 rabbit units are given, it is possible to continue pregnancy in cases which would otherwise have aborted. It would appear, therefore, that there is an entirely new field open for clinical experimentation, and after these introductory remarks I shall be most interested to hear the opinions of gynæcologists and obstetricians on the type of case they would hope to benefit by the sort of preparations which the biologists and biochemists can offer.

In conclusion, one might offer a word of warning with regard to the indiscriminate use of Prolan. As we know, it is possible to convert the ovary of an animal into a solid mass of lutein tissue by the administration of this material, and it would appear to be an undesirable state of affairs to produce in women. Before sitting down, however, I should like to plead for carefully controlled observations in clear-cut cases, and the avoidance, as far as possible, of the indiscriminate use of these substances in unexamined patients complaining of amenorrhœa, menorrhagia or climacteric disturbances.

Discussion.—The PRESIDENT (Mr. VICTOR BONNEY) said that an important fact made clear by Professor Dodds was that though the hormones that regulated the genital cycle in certain animals had been almost or actually isolated, the problem of assaying their exact values, even under ideal laboratory conditions, was only partly solved. When instead of on laboratory-controlled rats and mice, it was sought to assay their effect on women, the difficulties were so great as to be, for the present at least, insurmountable.

It was also evident that, having regard to the relative weight of a woman and a mouse, the administration of one of these really active hormones to a woman, in adequate dosage, would cost a sum of money that was prohibitive.

He hoped that Professor Dodds's paper would act as a corrective to that credulous optimism which, invariably assuming that "post hoc" was necessarily "propter hoc" resulted in the production of a number of worthless papers and an immense amount of worthless therapy.

Dr. A. S. PARKES discussed the standardization of extracts from the sex glands. (Estrus-producing hormones could be standardized to 10%; a certain dose would produce cornification of the vaginal epithelium, but a much larger dose was required to produce the other signs of œstrus. The amount required to produce signs of œstrus in various animals seemed to vary with the weight of the animal. For instance, it required 200 units to produce full œstrus in a mouse, and 100,000 units in a baboon, and assuming that a woman was equal to five baboons, it would require half a million units to get the effect in a woman; and for a cow it would require 5,000,000. To employ this amount of substance at the present time would be financially impossible.

Dr. H. GARDINER-HILL said that he had been provided by Professor Dodds with standardized extracts of œstrin for four years. This material had been tried out on cases of amenorrhœa. He had classified these cases into: (1) Primary amenorrhœa (normal individuals with delayed development, wasting diseases, and glandular defects); (2) primary menstrual irregularities, which were minor degrees of the first group, and (3) secondary

amenorrhœa. None of group 1, one-third of group 2, and in group 3 over half the cases of secondary amenorrhœa due to simple causes such as change of climate, shock, or pregnancy, had been affected. Secondary amenorrhœa due to glandular defect had been unaffected. Two cases were striking: both patients complained of amenorrhœa and sterility; both menstruated after injection of 180 and 200 mouse units respectively, became pregnant and had normal children. He (Dr. Gardiner-Hill) thought that preparations of œstrin such as those provided by Professor Dodds, were worth further clinical trial in carefully selected straightforward cases of amenorrhœa of the type he had discussed. He realized the difficulty of assessing clinical results in these conditions, but nevertheless thought that it was difficult to account for the changes in his cases except on the supposition that they had in some way resulted from treatment with œstrin. When the relative size of the human being and the experimental animals were taken into consideration the effective dose certainly seemed to be small, but the œstrus-producing effect in animals, mentioned by Dr. Parkes, appeared to be quantitative. Could not the clinical results be explained on the "trigger" hypothesis of W. Shaw—a small dose stimulating a sub-functioning follicular apparatus to produce active follicles and so initiating the cycle which ultimately resulted in the menstrual discharge?

Dr. J. M. ROBSON said that in Edinburgh they were carrying out a series of clinical observations, and enunciated the theory that once in the second half of the menstrual cycle the muscle was normally insensitive to the pituitary secretion, but that in these cases of dysmenorrhœa it became sensitive again before the endometrium had become properly disintegrated, with the result that painful contractions were set up.

Dr. T. C. CLARE suggested the possibility that the presence of hormones in the urine was not necessarily due to an increased secretion of hormones, but to the absence of fixation of hormones that had been secreted. He asked if any observations had been made on the presence of the Zondek reaction in patients who had recently had double ovariotomy performed. Theoretically, the reaction should be positive in such a case.

Rhabdomyosarcoma (Grape-like Sarcoma) of the Cervix. Specimen.—T. G. STEVENS, F.R.C.S.

Mr. T. G. Stevens showed a specimen of rhabdomyosarcoma of the cervix, removed from a patient aged 23. Slight bleeding between the periods for a year finally led the patient to seek advice. The growth was the size of a tangerine orange, attached by a pedicle half an inch in diameter to the vaginal cervix. There was no infiltration of the cervical tissues at all. Panhysterectomy with removal of both ovaries and tubes was performed. Fourteen days later a full treatment by deep X-rays was given. Microscopically the tumour showed spindle-celled sarcoma with strands of narrow striated muscle bundles and occasional strands of smooth muscle tissue. There was no cartilage present and epithelial pearls were not found.

Dr. F. J. MCCANN said that this was a specimen of great interest, showing the presence of striated muscle in a sarcoma of the cervix uteri. He (the speaker) had exhibited at a meeting of this Section a specimen of grape-like cervical sarcoma which contained cartilage, and he had removed another of the same type in which no cartilage was discovered. He had operated on four additional cases of cervical sarcoma, but in each there was recurrence of the disease at varying periods of time. He would be interested to know the after-history of Dr. Stevens' patient, for the prognosis in the recorded examples of cervical sarcoma was bad.

Section of Orthopædics.

[*November* 3, 1931.]

Two Cases of Spondylolisthesis.—B. H. BURNS, F.R.C.S.

Case I.—Mrs. P., aged 28.

First noticed lump in small of back whilst pregnant with second child in August, 1928. No particular trouble with either parturition. Pain was not felt till October, 1930, when it began in the lumbar region. In February, 1931, pains and cramp were felt in the calves and especially the right ankle. She found it impossible to stand for long on account of the pain in the back.

The trunk seemed shortened and the waist relatively high. There was a prominence of the upper part of the sacrum and a hollow space above this. Here there was some tenderness. There was some restriction of movement in all directions. The reflexes were normal and there was no demonstrable change in sensation. Antero-posterior skiagram showed a tilting upwards of the fifth lumbar spinous process (fig. 1). Lateral skiagram showed the fifth lumbar vertebra displaced forward about 5 in. on the sacrum (fig. 2).

On June 8 an Albee type of fusion operation was performed. A stout graft was taken from the tibia and inserted into the split spines of the third, fourth, and fifth lumbar vertebræ and first and second sacral spines.

The patient was kept on a plaster bed for three months and afterwards walked in a support for one month.

All pain has now gone and she has resumed normal activities.

Case II.—C. D., male, aged 48.

In March, 1931, in Birmingham a crane collapsed and fell on his back pinning him on the ground. He was taken to Hospital and kept recumbent for six weeks and then discharged in a plaster jacket. Since then he has been walking with difficulty and finds that progress is better when he leans forward supported by two sticks. He has pain in the lumbar region of the back which is not severe and does not keep him awake at night. Lately he has been getting pain in the calf of his right leg.

On examining the back there is a well-marked groove above the "step back" at the upper part of the sacrum and he is tender here. Hyperextension of the spine is most painful. Flexion is limited and somewhat painful. The reflexes and cutaneous sensations are not altered.

Skiagrams show a displacement forward of the body of the fifth lumbar vertebra on the sacrum (figs. 3 and 4).

Case II is obviously traumatic but there is no history of trauma in Case I. The pain in the calf was a conspicuous feature in both cases but in Case I it disappeared entirely six weeks after operation, while the patient was in a plaster bed.

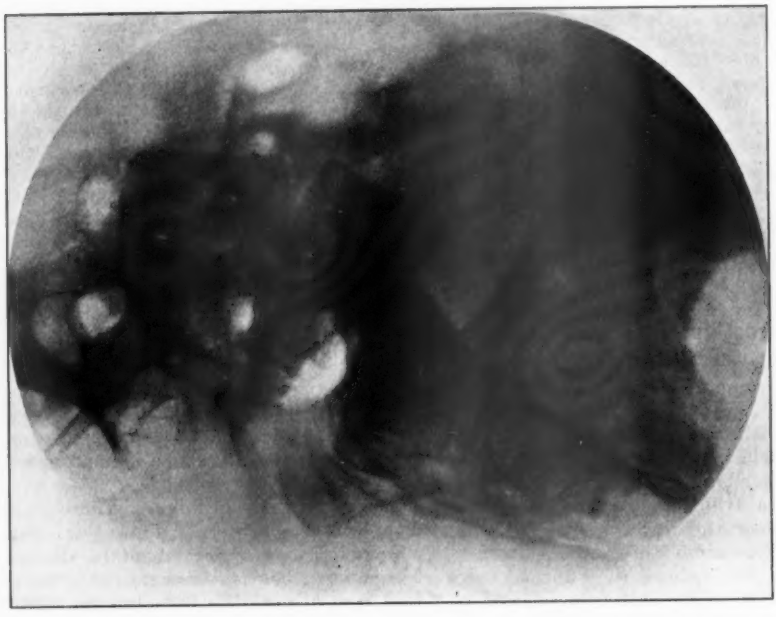


FIG. 2 (*Case I*).—Lateral view.

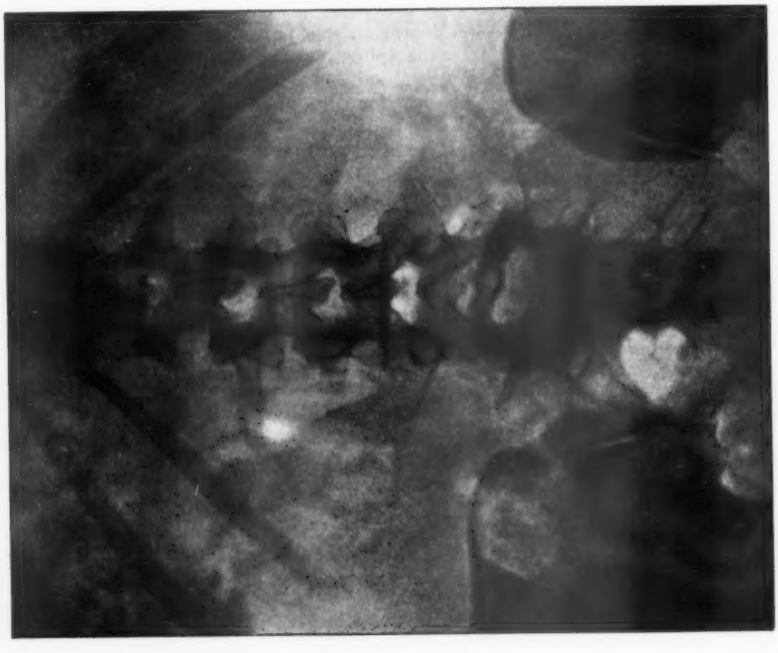


FIG. 1 (*Case I*).—Antero-posterior view.

FIG. 4 (*Case II*).—Lateral view.

FIG. 3 (*Case II*).—Antero-posterior view.

Osteitis of the Tarsal Scaphoid (Bilateral). ? Cause.—ERIC I. LLOYD, F.R.C.S.

2.2.31.—J. D., aged 8. History of six months' intermittent pain and swelling, left foot. On examination there was slight swelling and tenderness over the scaphoid such as occurs in Köhler's disease.

Skiagram negative; scaphoid normal (figs. 1 and 2).

FIG. 1.—Left foot, 2.1.31. Skiagram normal, in spite of a history of six months' pain and swelling over the left scaphoid.

FIG. 2.—Right foot, 2.1.31. Normal. No symptoms. (Control skiagram.)

Walking plaster applied and remained on for ten weeks. Pain was only partially relieved.

11.5.31.—On removal of plaster the indefinite swelling was a little more obvious and there was an inch of wasting in the calf. Mantoux test 1 : 1000 negative.

Skiagram showed slight general rarefaction and irregular upper border of left scaphoid (figs. 3 and 4).

FIG. 3.—Left foot, 11.5.31. The upper border of the scaphoid now has an irregular outline but the scapho-cuneiform joint remains normal.

Split plaster applied and crutches ordered. Removal of septic teeth and tonsils advised.

September 1931.—Pain and occasional swelling of other (i.e. right) foot.

October, 1931.—The left scapho-cuneiform joint now appeared to be disorganized and the joint space almost obliterated. Skiagram shows condition of right scaphoid exactly similar to that shown in left foot five months previously (figs. 5 and 6).

Wassermann reaction : negative. Mantoux test still negative.

FIG. 4.—Right foot, 11.5.31. X-ray appearances normal. No symptoms. This skiagram and fig. 2 were taken as controls and not on account of any symptoms in this foot at that time (see fig. 6, however).

FIG. 5.—Left foot, 13.10.31. Skiagram shows further advance in changes noted in fig. 3. An abnormal process runs distally from the upper border of the scaphoid and, though the astragalo-scaphoid joint is normal, the scaphoid-cuneiform articulation appears to be disorganised. Clinically, the child was better but began to complain of pain in the other foot.

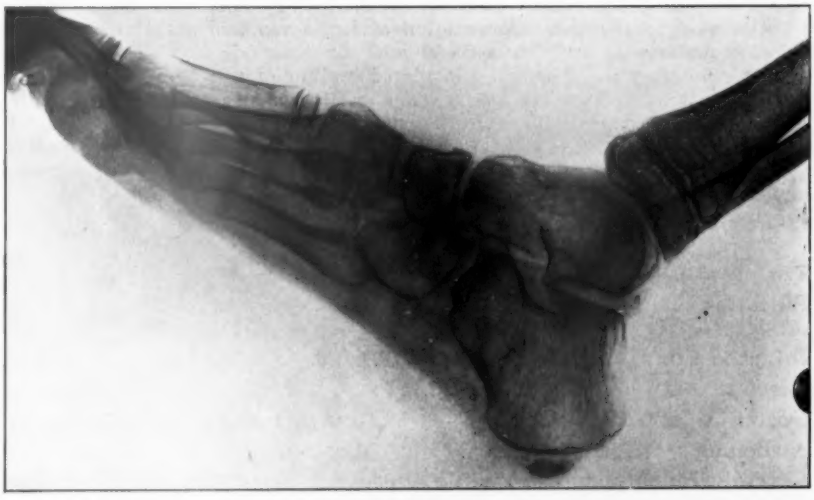


FIG. 6.—Right foot, 13.10.31. The upper border of the scaphoid now shows a strikingly similar appearance to that of the left foot, five months previously (see fig. 3). The patient now complained of pain in the right foot but the left was very much better. Since this time the child has been walking without restriction and with very little disability.

Sarcoma of the Foot.—B. WHITCHURCH HOWELL, F.R.C.S.

Married woman, aged 39, with four children. No history of tuberculosis or venereal disease. Swelling of the soft structures of the right foot, getting larger, especially lately. Varies in size, sometimes hot, always painful. Onset doubtful: probably in 1928.

Skiagrams show erosion of plantar surface of the os calcis and cuboid, apparently along the plantar muscles (see fig.).

SARCOMA OF FOOT.
Erosion of plantar surface of os calcis and cuboid.

Operation.—May 29, 1931.—Swelling explored and found to be like mulberry jelly. Obviously malignant. Amputation of leg, seven and a half inch stump, immediately performed.

Pathological report.—" There is a lobulated swelling of soft consistency 4 in. by 2½ in. by 1 in. lying between the long tendons and the small muscles of the plantar surface of the foot. The swelling, purplish in colour, is everywhere encapsuled. It appears to have arisen just superficial to the long flexor tendons, from their sheaths. The growth has not infiltrated any of the adjacent structures. Section shows a myxosarcoma."

Progress.—October, 1931. Patient alive and well.

The following cases were also shown :—

Pulsating Tumour in Groin : ? Diagnosis.—E. LAMING EVANS, C.B.E., F.R.C.S.

Infantile Coxa Vara.—ERIC LLOYD, F.R.C.S.

Cervical Rib.—T. K. LYLE, M.R.C.P.

Posterior Interosseous Palsy.—D. MCCRAE AITKEN, F.R.C.S.

Madelung's Deformity.—A. H. TODD, M.S.

Several Patients with Infantile Paralysis, after Tarsectomies done on the Lambrinudi principle.—C. LAMBRINUDI, F.R.C.S.

Fractured Pelvis.—PAUL BERNARD ROTH, F.R.C.S.

Arthrodesis of the Ankle, for Mal-united Pott's Fracture.—C. HOPE CARLTON, M.C., M.Ch.

Irregular Growth at the Lower Radial Epiphysis, following Trauma.—E. P. BROCKMAN, M.Ch.

[*December* 1, 1931.]

Cerebral Diplegia—Its Classification and Prognosis.

By REDVERS IRONSIDE, M.B.

I PROPOSE in this short paper to deal solely with the group of symmetrical cerebral diplegias which constitute by far the largest proportion of the infantile spastic palsies, 235 out of 280 such cases investigated by Ford at the Johns Hopkins Hospital.

I will attempt to divide these widely differing paralyses into groups, giving some neuro-anatomical basis for the classification, and to indicate some of the causes of the tremendous differences in the clinical appearances and treatability of the cases.

PATHOLOGY.

(1) In a small group the brain shows *arrested development.* This is chiefly evident in the cortex which presents a convolutional pattern more primitive than that which is normally established about the seventh month of fœtal life [1].

(2) In some cases the brain and spinal cord have been apparently *normal* to the naked eye ; but as most of the brains were studied before the introduction of modern histological methods, too much weight should not be attached to the absence of pathological microscopic changes [2-8].

(3) The commonest condition found post mortem, however, is *atrophic sclerosis.* The convolutions are shrunken, with evidence of neuroblastic death and degeneration

and secondary gliosis. The pyramidal fibres may reach only to the medulla or the upper portion of the cord, or the tracts may be of normal extent but poorly developed. The cells of the bulb and mid-brain may be affected. The distribution of the lesion

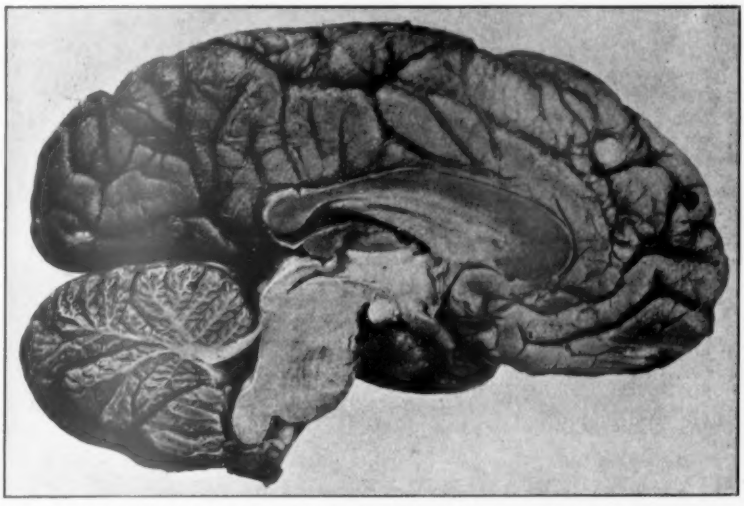


FIG. 1.—Mesial aspect of the left cerebral hemisphere from a male, aged 7½ years, a case of congenital spastic paraplegia, showing atrophic sclerosis of the paracentral convolution and atrophy of the posterior third of the corpus callosum. (From the Gordon Museum, Guy's Hospital.)

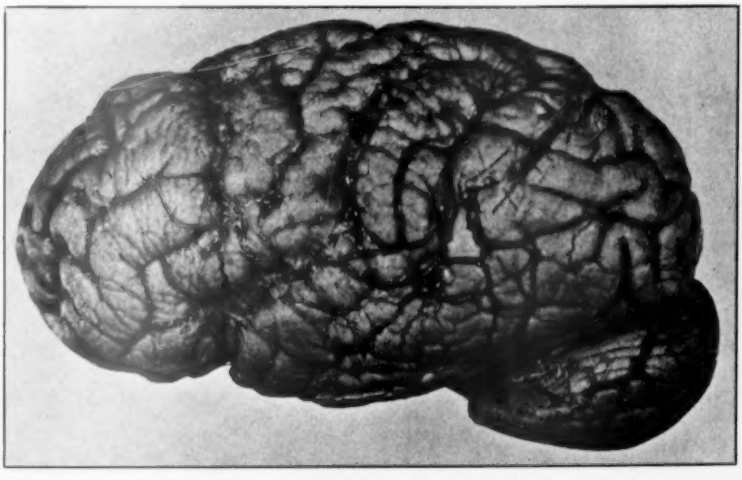


FIG. 2.—Lateral aspect of the same hemisphere, showing that the atrophic sclerosis is more scattered in the parietal, temporal and frontal lobes.

varies in the cortex but is strikingly symmetrical in the two hemispheres. In its *localized* form the paracentral lobules are chiefly affected, producing a paraplegia (figs. 1 and 2). The distribution may be *scattered*, the changes predominating in

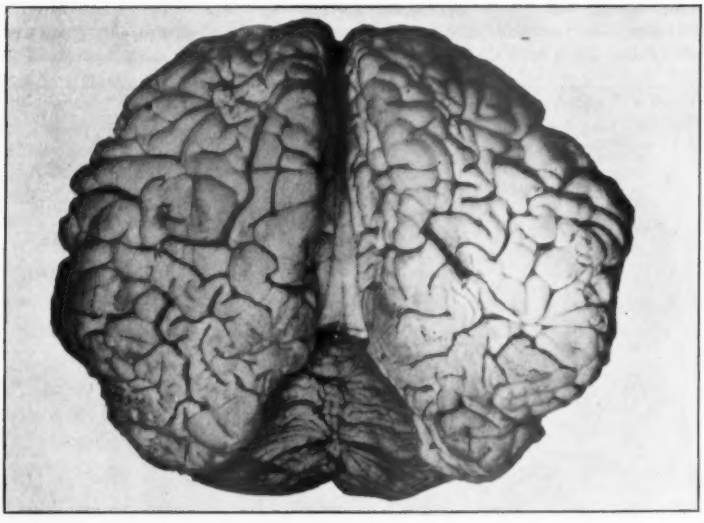


FIG. 3.—A "walnut brain" showing diffuse cortical atrophic sclerosis. The frontal and occipital gyri were hard, shrunken and leathery, while the cerebellum was normal. From a male, aged 14 weeks, normal full-time labour—4 lb. at birth. Convulsions, general rigidity, inability to swallow and blindness. Death from diarrhœa. (From the Hospital for Sick Children, Great Ormond Street.)

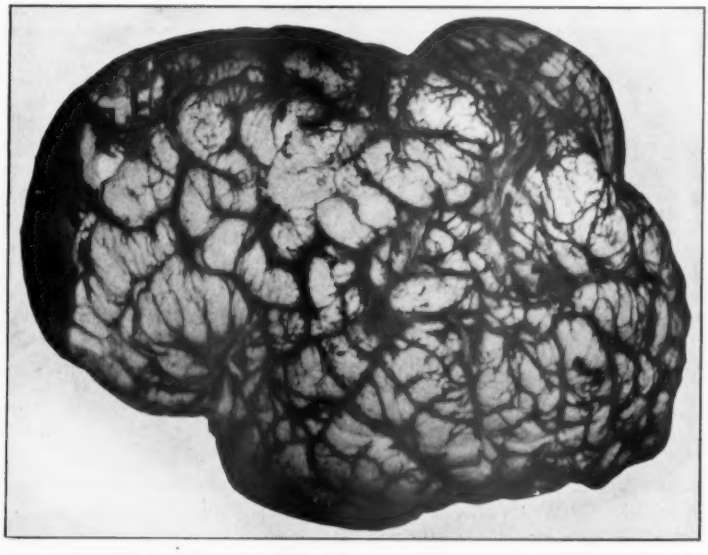


FIG. 4.—The brain of a diplegic child, aged 1 year 10 months. The membranes show kinking and opacity, especially over indentations of the cortex near the vertex, where large leashes of vessels are apparent. (From the Hospital for Sick Children, Great Ormond Street.)

the pre-frontal lobes or in the temporal or parieto-occipital lobes, producing mental defect and even cortical blindness. In its *diffuse* form atrophic sclerosis produces the condition of " walnut-brain " (fig. 3).

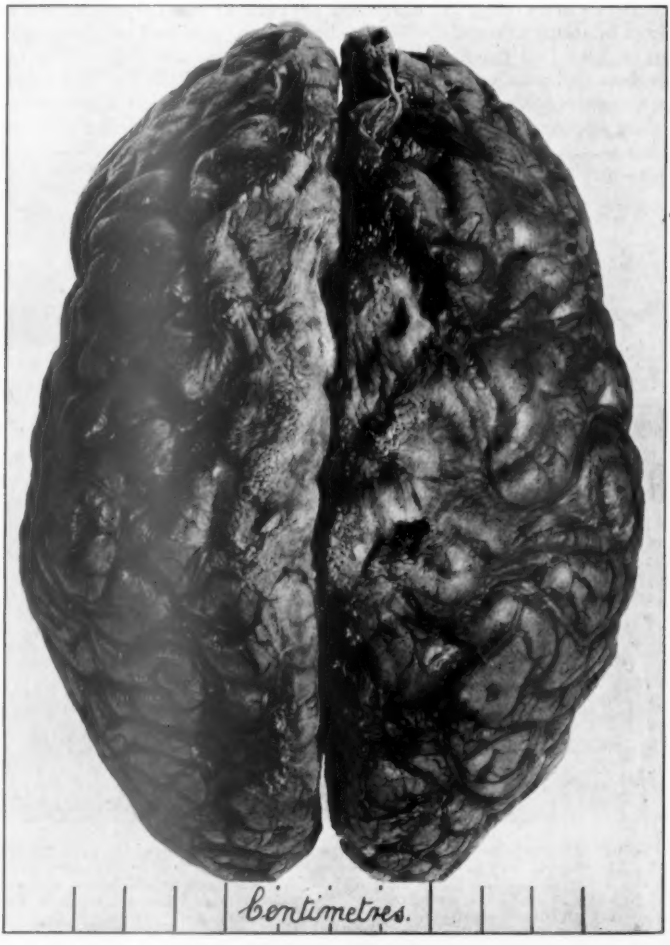


FIG. 5.—The brain of a diplegic, aged 41 years, who died from pulmonary œdema and myocardial degeneration, showing marked symmetrical thickening of the pia-arachnoid over the middle third of the great longitudinal fissure. Dura mater normal.

The frontal lobes are poorly developed, with a simple convolutional pattern. A depression is seen at the mesial end of the parieto-occipital sulcus. The corpus callosum is small. The cerebellum, pons and medulla showed no abnormality. The pyramids are fairly well developed. The disease was apparently pre-natal, the lower limbs were spastic and contractured and the mental age approximately five years. (Dr. R. M. Stewart's case.)

Exactly analogous changes to those seen in the cerebrum may affect the cerebellum. Molecular disintegration of masses of neuroglial overgrowth may cause the formation of porencephalic cavities, and from disappearance of cerebral substance the

ventricles may be comparatively enlarged (hydrocephalus ex vacuo). The pathological changes appear to commence in the deeper layers of the cortex and it is difficult to reconcile the morbid anatomy with any theory of birth injury being its cause.

(4) In 1911 Cecile Vogt [9] described changes in the corpus striatum in a case of congenital bilateral athetosis. These changes are confined to the caudate nucleus and putamen, and had been previously observed by Anton [10]. The cells of the caudate nucleus and putamen are atrophied and to the naked-eye the corpus striatum, in Weigert myelin-stained preparations, presents a mottled appearance, the *état marbré*. The apparent enlargement of the internal capsule is due to disappearance

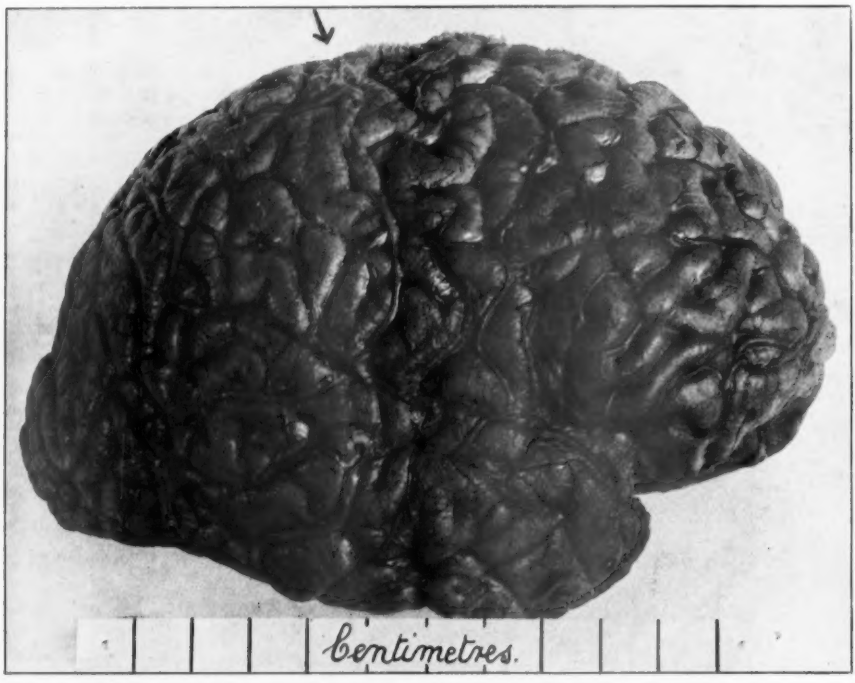


FIG. 6.—From a male case of congenital spastic paraplegia, who died aged 17 years, from acute miliary tuberculosis. The vein running down the sulcus centralis is broad, thickened, opaque and yellowish in colour. On the left cerebral hemisphere abnormal veins were found in situations corresponding to the posterior end of the first frontal convolution. The appearance of these vessels indicates previous venous thrombosis, probably occurring at birth. The pyramids are very poorly developed. Labour was prolonged and the child was born asphyxiated, delivered by forceps. Mental age of three years. Incontinent, with fits and an internal squint. (Dr. R. M. Stewart's case.)

of a large part of the corpus striatum. In a recent article the Vogts state that they regard the condition as the result of a pre-natal process. The condition is associated clinically with congenital bilateral athetosis and chorea.

(5) In another group of cases the membranes show much kinking and opacity, and there are marked depressions at intervals over the surface of the brain (figs. 4 and 5). The cortical and meningeal vessels are deformed and there may be evidence of peri-arteritis or perivascular neuroglial sclerosis. Cortical venous thrombosis may be found (fig. 6).

No ætiological classification seems to be possible in the present state of our knowledge. Nearly all the pathological material available is late and may be the result of several initial causes, e.g., congenital arrest of development, anoxæmia during fœtal life or during delivery, fœtal encephalitis or toxæmia.

Classification.

In true prenatal cases the disease is usually noticed at birth or within the first few weeks of extra-uterine life. In post-natal cases the progress is apparently normal until a few months after birth when it is noticed that the child is becoming rigid, does not hold up the head properly or there are convulsions. There is a good deal of clinical evidence that in the pre-natal cases the disease is often stationary or tends to improve, while most of the post-natal cases show a progressive course. It seems useful to distinguish the two groups. Very rarely, familial post-natal cases are seen affecting the siblings of one generation.

(1) *Cortical types.*—Symmetrical: (*a*) Spastic paraplegia; (*b*) Spastic diplegia.

The disease is in the paracentral lobules or more scattered. Clinically, there is symmetrical spastic weakness affecting the legs more than the arms or the legs alone. In the most severe cases there is general rigidity of the extremities, often contractures and signs of bulbar involvement, while the mildest cases show only slight spasticity and a tendency to walk on the toes. The pupillary reactions may show various abnormalities, and in about one-third of the cases there is convergent strabismus. Blindness, either cortical or due to primary disease of the optic nerves, may occur.

(2) *Striatal types.*—Symmetrical: (*a*) Bilateral chorea; (*b*) Bilateral athetosis.

The disease is in the caudate nucleus and putamen. Bilaterally symmetrical choreic or athetotic movements occur in the limbs, trunk and facial muscles. The plantar responses are flexor.

(3) *Cortical-striatal types.*—Often asymmetrical.

These patients show a combination of bilateral pyramidal signs, most marked in the lower limbs, with involuntary movements, ocular palsies, bulbar signs and mental defect. The facies and attitude may be Parkinsonian. Involuntary movements may predominate on, or may even be confined to, one half of the body.

(4) *Cerebro-cerebellar types.*—Symmetrical.

The disease is in the cerebellum and its connections and the frontal poles. Clinically, the cases may show cerebellar ataxia, cerebellar speech, nystagmus and atonia [11], with absence of tendon reflexes. Signs of pyramidal involvement may be present.

The types outlined above are not absolutely defined and transitional cases occur.

From the motley group of diplegics, within recent years several conditions of different pathology have been separated.

(1) *Double hemiplegias*, perhaps due to birth injuries, when the arms are more severely affected than the legs, the distribution asymmetrical and the infant's head large. In true diplegia the converse is true. Double subdural hæmatoma in infants, the so-called hæmorrhagic pachymeningitis, apparently causes no paralysis, or in a few cases a monoplegia or hemiplegia only. Rare instances may be found in the literature of diplegia resulting from thrombosis of the superior longitudinal sinus.

(2) *Spinal cord birth injuries*, without vertebral fracture, can occur from traction on the child during labour. Many of the cases are breech presentations and show hæmorrhage, either extra-thecal, subdural, subarachnoid, or into the cord itself. Most die at birth, but a few survive with signs of an incomplete transverse lesion of the cord [12, 13].

(3) *Amaurotic family idiocy*, with its characteristic cherry-red spot at the macula and the *Juvenile form of cerebro-macular degeneration* [14], with its "pepper and salt" macula. Transitional forms are found between these, the diplegias and the Merzbacher-Pelizaeus disease.

(4) *Congenital hydrocephalus*, due either to congenital malformation of the aqueduct, sealing up of the aqueduct by inflammatory exudate or plugging of the aqueduct with organized blood-clot subsequent to intraventricular birth hæmorrhage.

Encephalography.

Diagnostic lumbar puncture, Wassermann reactions in blood and spinal fluid, and ordinary X-ray examinations of the skull are almost uniformly negative, although they should always be performed. Encephalography, or the fractional replacement of spinal fluid by air and subsequent X-ray, gives additional information about the ventricles, the subarachnoid space and even convolutional markings, and might be considered a fruitful kind of investigation [15, 16].

I have found the procedure of little use in dealing with diplegic children, although I have used it courageously in spite of severe meningeal reactions lasting for days, and in the face of reported deaths. It is difficult to show convolutional markings without inducing dangerously increased intracranial pressure. The accommodation of air in the subarachnoid space is an affair which shows much variation in the normal, and an apparent increase in depth of the subarachnoid space, particularly in the frontal regions, should not rashly be attributed to lack of cerebral substance there. Symmetrical slight dilatation of the ventricles (hydrocephalus ex vacuo) or absence of filling of the ventricles with air are found in a few cases.

The results are more instructive in asymmetrical brain lesions, e.g., the infantile hemiplegias. Porencephaly, cerebral or cerebellar agenesia may be demonstrated. Ventriculograms are occasionally necessary to make the diagnosis from hydrocephalus of one type or another.

Intelligence Testing.

In my work with the group of diplegic children at St. Vincent's Orthopædic Hospital, I have had the assistance of workers supplied by the Child Guidance Council, to whom I would express my thanks; especially to Dr. Moodie, Miss Lucy Fildes and Miss Allan. While gross mental deficiency can be recognized within the first few months of life, in slighter cases the intellecual level of the child is more difficult to establish. The question is of the greatest importance in prognosis, and the employment of intelligence tests I believe to be of the utmost assistance in forming an opinion. For children under five years we use the Merrill-Palmer scale, and for older children Burt's revision of the Binet scale [17, 18]. It is possible to fix the intelligence quotient and the mental age in many of the cases. By presenting a given series of these tests it is possible to compare one diplegic child with another, while no useful comparisons can be made with the normal. Five boys, selected at random from the group, whose ages ranged from $11\frac{1}{2}$ to $14\frac{1}{2}$ years, gave intelligence quotients of 85, 62, 59, 58 and 48. There is no relationship between the type and degree of physical disability and the amount of psychical failure. A child may be going downhill physically while the intelligence level is preserved. Intelligence tests are showing us that these children have interest and desire to succeed and power to concentrate, but they vary considerably in persistence. They tend to expect that things will be made easy for them or that less effort will be expected from them than from other children. If they find a task hard they will see no reason why they should wrestle with it. Most show failure in memory or memorizing. Many such children have been put to bed for long periods and isolated from social interests and educational methods, and it is hardly surprising that they show lack of grasp of everyday situations, defect of "common knowledge"

and vocabulary. Some show the phenomena of mirror-writing and mirror-reading. Repetition of intelligence testing at regular intervals is just as important as repeated physical examination.

The tragedy is that a general impression exists that the mental defect is severe in all cases. Speech defects and grotesque involuntary movements cause difficulty in exteriorizing ideas, and in competition with normal children diplegic children develop emotional disturbances, temper-tantrums, sensitiveness and fears. In the striatal group, emotional upset definitely increases the involuntary movements. I recently saw a boy of 9 years with a small cranium and generally unprepossessing exterior, suffering with a cortical type of diplegia. He had wild temper-tantrums in which he fought and scratched. On this account he had missed two years of schooling, was thought to be defective, and although his I.Q. was 98, such was his feeling of frustration and insecurity that in competition with children who were really his mental equals he felt unable even to begin to learn.

An attempt to assess, by scientific means, the intellectual level will help in solving such problems and in deciding whether the child is to be treated at home, at school, or in an institution.

Prognosis.

The neuro-anatomical classification given is of little help in prognosis. In a general way one may say that most cortical diplegias with paraplegic rigidity and slight mental retardation improve greatly, and that the cerebro-cerebellar cases mostly progress favourably under careful training. Assuming that the correct diagnosis has been made, the prognosis, in any given case, rather depends on (1) a careful assessment of the physiological residue of power, (2) the stationary or progressive character of the disease, (3) the intellectual level of the child, and (4) the presence or absence of epilepsy, blindness or incontinence. The physiological residue of power may be impaired by the presence of rigidity or contractures, inco-ordination or involuntary movements. Amelioration of symptoms is more likely to occur in pre-natal cases, where the lesion is apparently a fixed one. Intelligence testing should be routine in all cases, with special regard to the eagerness and persistence of the child and the ability to memorize; and attention should also be paid to the emotional stability and general behaviour. The occurrence of epilepsy is almost always a sign that the disease is to become progressive and is of the gravest omen. Incontinence usually goes with gross mental deficiency, and blindness invariably indicates a progressive type of cerebral defect. In my experience, the ability to demonstrate mid-brain postural reflexes has been found only in severe diplegias.

I am convinced that by studying each case in this way a sounder prognosis can be given than by reliance on any clinical or anatomical grouping. All these cases, in the absence of fits, gross mental deficiency, incontinence or blindness, should be regarded as interesting, soluble problems in education, rather than a dull, pitiful group of dependent cripples. One has only to see a large number of late cases of diplegia in any of our larger public institutions to be convinced of the value of orthopædic treatment in preventing deformities. If there is any reason for believing that neurologists are of little help in this disease it is partly because these problems of prognosis are not talked over sufficiently by the orthopædist and neurologist together, and partly because we tend to lose the obstinate sort of optimism that is necessary if we are to treat these children with success.

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Spontaneous Hyperæmic Dislocation of the Atlas.

By R. WATSON JONES, F.R.C.S., M.Ch.(Orth.).

ONE day in the course of her round, a nurse was dressing the sinuses in the neck of a girl aged 16 suffering from tuberculosis of the cervical glands with secondary pyogenic infection. In order to gain better access, the nurse pushed the patient's cheek with the back of her hand as she asked her to turn her head—the girl choked, became cyanosed, and was dead. Post-mortem examination revealed a forward dislocation of the atlas with compression of the cord by the odontoid process of the axis. This case, perhaps the most dramatic of its type, has been reported by Reid [1], and during the last few years, 12 other examples of spontaneous dislocation or subluxation of the atlas have been recorded by Swanberg [2], Berkheiser [3], Seidler, Grisel [4], Desfosses [5], and Grieg [6]. Although the condition is apparently little known and seldom recognized, it is just 101 years since Sir Charles Bell [7] described the case of a man with a deep ulcer on the back of his throat who sustained a dislocation of the atlas; in the words of Bell, "the ulcer had destroyed the transverse ligament of the atlas."

The condition is apparently rare, and this paper has been based on the fourteen previously recorded cases, as well as on the two cases which have occurred in my own practice and have been personally observed.

Ætiological factors.—It is of importance to note that the condition is almost confined to the first decade of life. In only three of the sixteen cases have the patients been older than 11, and the common ages are 8, 9 and 10.

AGE INCIDENCE. (ANALYSIS OF RECORDED AND PERSONAL CASES.)

Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Cases ...	1	...	...	...	...	...	1	2	4	2	1	...	...	...	...	2	...	...	...	...	...	1

SEX INCIDENCE.

Females 8 Males 6 Unknown 2

On no occasion has there been any real traumatic factor. As a rule the onset has been absolutely spontaneous, and the dislocation has been produced by a normal movement of the head. In Swanberg's case the dislocation had first appeared some hours after the operation of tonsillectomy, but in one of my cases it appeared four days *before* operation for acute mastoid disease.

The one predisposing factor which has been constant is the existence of an inflammatory focus in the upper neck. Grisel and Desfosses thought that the infection was necessarily nasopharyngeal in origin, and have therefore coined the term, "nasopharyngeal torticollis." More detailed study shows, however, that any infection which would cause hyperæmia in the region of the base of the skull may give rise to the condition—tonsillitis, pharyngitis, middle-ear disease, mastoid disease, inflamed cervical glands and so on. The type of organism responsible is of no significance—the infection may be pyogenic, tuberculous or syphilitic. Moreover, there need not be any direct association between the focus of infection and the atlas.

RECORDED CASES OF SPONTANEOUS DISLOCATION OF THE ATLAS.
CLASSIFICATION OF PREDISPOSING CAUSES.

Acute tonsillitis	4	Acute suppurative mastoiditis ...	1
Influenzal cold (nasopharyngitis) ...	3	Tuberculous cervical adenitis ...	1
Sore throat (pharyngitis)	2	Pyogenic cervical adenitis	1
Scarlet fever with pharyngitis ...	1	Cervical abscess (? retropharyngeal) ...	1
Syphilitic ulceration of pharynx ...	1	None known	1

Clinical features.—The history usually given is that the child was not well and had a cold or a sore throat. A week or ten days later for no apparent reason he suddenly complained of a "crick in the neck" and the mother noticed that his head was twisted and that movements were avoided. The head is held rigidly, slightly in front of its normal plane, tilted towards one shoulder, with the face rotated towards the opposite shoulder. It is, in fact, the ordinary position of any torticollis, but there is no contracture or spasm of the sterno-mastoid; the rigidity is apparently due to spasm of the deep cervical muscles. Any attempt to move the head is strongly resisted, and very much resented by the child, who moves cautiously, and will support his chin on his hands when rising from the recumbent position, or performing any movement which demands flexion of the neck. There is no tenderness over the cervical vertebræ, but percussion gives rise to pain. Skiagrams show a forward displacement of the skull and atlas on the axis. The odontoid process may lie as much as half an inch behind the anterior arch of the atlas and appears to be situated in the middle of the foramen magnum. In none of the cases which survived was there any evidence of an irritative lesion of the cord, although radiological examination makes it clear that the cord is lying in a very restricted space, between the odontoid and the back of the atlas and foramen magnum. It is clearly only a question of degree, the matter of a mere millimetre, which is separating life from death.

One feature of the greatest significance is that the anterior arch of the atlas may show marked decalcification. In the first of the author's cases, the pre-operation skiagram (fig. 1a) shows that about half of the anterior arch has completely disappeared, and if it were not for the subsequent skiagram one would suspect either a congenital anomaly, or actual bony destruction by tuberculous or pyogenic disease. The second skiagram, however, taken only three months later (fig. 1b) shows that the arch is once more intact, and its apparent disappearance has been due simply to decalcification.

Pathology.—Four important facts stand out clearly from the ætiological and clinical features.

(1) The condition is peculiar to children, at an age when the bones are imperfectly developed and not yet well calcified. (2) It is necessarily associated with an inflammatory lesion which may be situated anywhere in the upper cervical area. (3) There is a latent period of about from seven to ten days between the onset of infection and the dislocation. (4) The anterior arch of the atlas shows decalcification but not destruction.

The relationship of calcification of bone to its blood supply was not clearly understood until Grieg [6] of Edinburgh published his investigations. To him we owe the proof that hyperæmia causes decalcification of a bone, and reduction of the blood supply causes sclerosis. With this fact established, it is easy to appreciate the sequence of events in spontaneous dislocation of the atlas. The focus of infection is responsible for an ever-widening area of hyperæmia. If the focus is anywhere in the upper cervical area the field of hyperæmia will eventually include the upper cervical vertebræ and particularly that part of the atlas which is nearest to the infection. In pharyngeal infections this is the central part of the anterior arch of the atlas, and in mastoid infections the lateral part of the arch of the atlas on the same side as the mastoid (fig. 1). Decalcification is now inevitable. After a latent period of from seven to ten days in an average case of pharyngeal or tonsillar infection,

FIG. 1A.—Spontaneous dislocation of the atlas in a boy aged 9, five days after onset of symptoms of acute mastoid disease. Note that half of the anterior arch of the atlas has "disappeared" owing to hyperæmic decalcification.

FIG. 1B.—Same case as fig. 1A, four months later. Dislocation is now fully reduced and the atlas is completely re-calcified. There was perfect recovery with a normal range of movement of all joints.

FIG. 2A.—Spontaneous dislocation of atlas in a child aged 2. In this case the hyperæmia was secondary to a simple "cold in the head" with pharyngitis.

FIG. 2B.—Same case as Fig. 2A. Complete recovery in 4 months.

the degree of decalcification is such that the arch of the atlas no longer affords a secure attachment for the transverse ligament, which is mainly responsible for maintaining the odontoid process in close relationship with the atlas. A normal movement of the head may avulse the ligament and allow forward displacement of the atlas. According to the degree of avulsion, the dislocation is complete and the patient dies suddenly, or is incomplete and the syndrome we have described is established (figs. 1A, 2A).

Treatment.—Recorded cases have been treated, as a rule, by recumbency and head extension, and in many cases prolonged fixation has been deemed necessary. Berkheiser and Seidler maintained traction and then fixation for as long as twelve months, presumably because they considered the condition to be due to an infective process in the atlas and atlo-axoid joints.

Knowing, as we now do, that the dislocation is purely mechanical in origin and due to decalcification of the atlas, it is clear that prolonged fixation is not only unnecessary but not advisable, since it will give rise to still further decalcification by atrophic change.

Provided that the dislocation is not of long standing, it may be reduced with the greatest ease by simple hyperextension of the head (figs. 1B, 2B). Under an anæsthetic the muscle spasm disappears, the neck is fully extended and the head, neck, and upper trunk are put up in plaster. It is found that all discomfort, pain and fear of movement are relieved at once, and the patient need not be recumbent for more than 24 hours. Energetic steps must be taken to secure quiescence of the infection, and a sufficient time allowed for the hyperæmia to subside and the atlas to recalcify. In both of my cases the plaster was retained for 10 weeks. After re-educative exercises for two months a full recovery was made—there was a normal range of movement of all joints, no deformity, no pain and the X-rays showed complete recalcification.

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